

A close-up photograph of a young child with dark skin and short hair. The child is looking off to the side with a curious expression. They are holding a light-skinned doll with a textured, brown, fibrous headpiece. The child's mouth is open, and they appear to be biting or holding the neck of the doll. The child is wearing a patterned garment with blue, orange, and white colors. The background is a plain, light-colored wall.

**III. Advancing and sharing
chemicals management
tools and approaches:
taking stock, looking into
the future**

About Part III

In Part II a range of initiatives by countries, international organizations and other stakeholders to achieve sound management of chemicals are described. Part III provides insights into the progress made, as well as gaps and opportunities concerning science-based approaches, tools, methodologies and instruments used in managing chemicals to protect human health and the environment. Valuable lessons have been learned over the past decades in the practical application of these approaches, tools, methodologies and instruments. In addition, opportunities have emerged to enhance their effectiveness, simplify their use, and employ them more systematically in all countries.

The order of the chapters in Part III generally follows the chemical risk assessment and risk management process. That process leads from hazard assessment to exposure assessment, risk assessment, and risk management and alternatives assessment. Later in Part III, special attention is given to chemical risk management in small and medium-sized enterprises (SMEs) and the informal sector in developing countries – including the challenges faced and opportunities to improve chemical safety in these settings.

Part III concludes with a forward-looking chapter (Chapter 8) on assessment approaches that consider a life cycle perspective and broader sustainability criteria. Throughout Part III, specific suggestions are made concerning ways that countries with limited resources could benefit from considering scientific work undertaken in other countries that have more advanced chemical management schemes.

Governments are the main drivers of the risk assessment and risk management approaches presented. However, Part III also addresses a range of work in (and results generated by) international organizations, which bring together governments and other actors, particularly industry, to identify opportunities for collaboration and foster harmonized approaches. These organizations include the World Health Organization (WHO) and the United Nations Economic Commission for Europe (UNECE), which serve as the secretariat for the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Furthermore, the Organisation for Economic Co-operation and Development (OECD) leads a range of technical work to harmonize methods and approaches that are used in its 36 member countries and in many other countries. Global risk assessment and management actions on chemicals of global concern are facilitated through a number of legally binding and soft law instruments, several of which are serviced by the United Nations Environment Programme.

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1/ Hazard assessment: progress in information generation and hazard characterization

Chapter Highlights

Harmonization of test methods saves resources and reduces the need for animal testing.

Important progress and efficiencies are being obtained through the use of new methodologies based on the grouping of chemicals.

Hazard classification criteria have been developed in the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). However, achieving globally harmonized hazard classifications of chemicals has proven more challenging.

Efficiencies can be obtained through global sharing and acceptance of hazard assessments undertaken at the national or regional level.

All of the actions above would result in major efficiencies for all actors concerned, but would benefit, in particular, countries with limited resources.

Chemical hazard assessment is the first stage in the risk assessment and risk management process. This chapter summarizes advances in the approaches and methods that are used to generate chemical hazard data and to assess chemical hazards globally. It also identifies gaps and points to opportunities to accelerate chemical hazard assessment.

Chemical risk assessment has been described as a systematic process that is “intended to calculate or estimate the risk to a given target organism, system or (sub) population, including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system” (OECD 2003). It comprises four steps: hazard identification, hazard assessment (also called

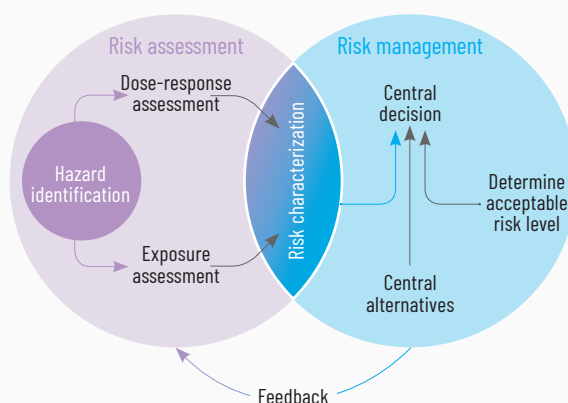
“hazard characterization” or “dose-response assessment”), exposure assessment, and finally risk characterization. Risk assessment is followed by risk management decision-making and by the implementation of risk management measures, if these are considered necessary.

1.1 Drivers for the generation of hazard information

What are chemical hazards?

The term chemical hazard refers to the intrinsic properties of chemicals which have the potential to cause adverse effects on human health and the environment. Examples of such properties include: acute toxicity; corrosive properties; the ability to bring about allergies; long-term effects on reproduction, development and other

Figure 1.1 From risk assessment to risk management (adapted from United States National Library of Medicine 2018, image source: Oak Ridge Associated Universities®)



systems in the human body; and persistence in environmental media. A hazard assessment is a qualitative and – where possible – quantitative description of the adverse effects of a chemical, based on generated information (American Chemical Society 2018; Swedish Chemicals Agency [KEMI] 2018). Many factors can influence the impacts of exposure to a chemical. These factors include the dose and duration of the exposure, the kinetics of the chemical in an organism, and the susceptibility of the exposed organism.

Who generates chemical hazard information?

Given the size of the global chemicals market and the potential of many chemicals to cause harm, there is broad consensus internationally that more hazard information is needed to allow meaningful hazard assessments to be made. National, intergovernmental, industry and other initiatives to identify chemical properties in order to carry out hazard assessment include:

- › *Regulatory requirements:* In many countries a minimum set of information on new chemicals – as defined by national jurisdictions – and on priority existing chemicals already on the market is required by chemical safety



legislation. Such legislation exists, for example, in Canada (Government of Canada 2016a), the European Union (EU) (European Commission [EC] 2006; European Chemicals Agency [ECHA] n.d. a), Japan (Japan Ministry of Economy, Trade and Industry 2016) and the United States (United States Environmental Protection Agency [US EPA] 2018a; US EPA 2018b).

- › *Testing of new chemicals in the development stage:* In the development stage of new chemicals, producers often use predictive methods such as quantitative structure-activity relationships (QSAR) and screening to identify hazardous properties of candidate chemicals, or to perform screening risk assessments for these chemicals' intended uses. As chemicals move from the research and development phase to production, additional testing is often performed to obtain better knowledge for use in deciding whether (and which) risk reduction measures will be needed to adequately protect workers involved in their production and use and to protect the environment (Maertens *et al.* 2014).
- › *Research programmes:* Extensive testing of the mechanisms of toxicity of chemicals takes place in research programmes, for example to develop test methods for new types of substances whose impacts on human health and the environment are not yet fully understood, such as nanomaterials (US EPA 2016; Gottardo *et al.* 2017; EC 2018; OECD 2018a) or to investigate newly identified effects, as in the case of endocrine disruptors (Beronius *et al.* 2014; US EPA 2017).

important area of OECD work. This includes precise characterization of the test substance and ensures methods' reproducibility and transferability (OECD 2005). The Test Guidelines developed by the OECD are the most complete set of international standards for chemical hazard testing for regulatory purposes. They include methods to determine physical-chemical properties, ecotoxicity, fate and behaviour in the environment, and mammalian toxicity (OECD 2018b; OECD 2018c; OECD 2018d; OECD 2018e). Quality control is ensured through the OECD Principles of Good Laboratory Practice (GLP) and the GLP compliance monitoring system (OECD 2018f). The OECD Test Guidelines are continuously updated and further developed. For example, for technically challenging substances such as nanomaterials the OECD is currently working on a set of standardized Test Guidelines for, inter alia, precise characterization to enable appropriate testing and assessment of these substances (OECD 2018g).

Through international standardization and harmonization of test methods, resources needed for chemical hazard assessment can be significantly reduced: chemicals need to be tested only once, after which the results will be accepted in many other countries (OECD 2018h). The OECD's system of Mutual Acceptance of Data (whereby test results generated according to the OECD Test Guidelines and the OECD Principles of GLP are in principle accepted in 42 OECD and non-OECD countries) was already estimated in 2010 to save governments and industry about euros 150 million per year (OECD 2010). Avoiding duplication of testing also significantly reduces the use of animals in testing (OECD 2018i).

Harmonization of test methods saves resources and reduces use of animals



To support regulatory requirements in member countries of

the Organisation for Economic Co-operation and Development (OECD), standardization of test methods has been identified as an

1.2 Test methods to identify chemical hazards are evolving rapidly

Animal testing provides important information, but progress is being made on non-animal test methods

Chemical testing has traditionally been carried out on animals (e.g. rats, mice and fish). Through the use of laboratory animals, insights can be

obtained into the toxicological effects a chemical could have on humans or wildlife. For certain more complicated toxicological endpoints, such as carcinogenicity and effects on the reproductive system, this type of testing can be costly, requires large numbers of animals and raises ethical concerns. While such testing may be required by statute, it is usually conducted for chemicals which are a priority due to their high production volumes, their wide use, or the expectation that they have hazardous properties of particular concern (e.g. are carcinogenic).

Reducing, refining and replacing test methods that use laboratory animals has been a priority in many countries for many years. In particular, since the publication of the report *Toxicity Testing in the 21st Century: A Vision and a Strategy* (United States National Academy of Sciences 2007), governments have increased their efforts to move towards the adoption of alternative test methods such as systems using cell cultures (*in vitro* methods) instead of animals (*in vivo* methods) (Krewski *et al.* 2010). The most recent developments in this field include high-throughput screening and toxicogenomics and RNA sequencing methodologies. An example of work being carried out is the US EPA's ToxCast programme, which includes publicly available

high-throughput toxicity data on thousands of chemicals (US EPA 2018c). High-throughput screening results are especially useful in setting priorities for further work to investigate hazards. Another approach with significant potential to replace animal testing is *in vitro* embryonic stem cell research (Colaïanna *et al.* 2017; Cynober 2018).

Guidance on the use of non-animal testing approaches under relevant European legislation has been developed by the ECHA (ECHA 2017a; ECHA 2017b; ECHA 2017c). In the United States new approaches and alternative methods for use in a regulatory context are developed and evaluated (US EPA 2018d; United States Interagency Coordinating Committee on the Validation of Alternative Methods 2018). Many of the new testing methods are not direct replacements for *in vivo* tests. Instead, they require countries to accept different approaches to hazard identification for regulatory purposes (see also section 1.3 below). Considerable progress has been made in the international development of methods that do not require the use of animals in testing. However, it is expected that this (often expensive) type of testing will continue to be needed in the coming decade, particularly for long-term toxicity endpoints.



What are current opportunities for global acceptance of test data?

As discussed in Part II, a number of countries are establishing regulatory frameworks or upgrading frameworks already in place in order to advance sound chemicals management – including through provisions concerning data requirements. These initiatives often focus on industrial chemicals, as well as on consumer uses of chemicals which are not regulated elsewhere. Examples of regulatory initiatives that involve requests for data submissions for a large number of chemicals include those in China (initiated in 2003 and amended in 2009) (Chemical Inspection and Regulation Service [CIRS] 2017; Lexology 2018), the Republic of Korea (CIRS 2012a; ChemSafetyPro 2017; ChemSafetyPro 2018; He 2019) and Turkey (CIRS 2012b; SGS 2017). As part of these initiatives, countries usually request data from both producers and importers and may therefore ask for testing.

Hazards are intrinsic chemical properties which are the same in all countries. Global acceptance of test data is, in principle, possible and desirable provided there is full transparency concerning the test methods used and the limitations of these methods. Wide acceptance of test data could provide efficiency gains and make resources available for testing more chemicals than is currently possible. Any country that requires (or plans to require) the generation of data by chemical producers and importers for hazard assessment and risk assessment could therefore consider joining the OECD's system of Mutual Acceptance of Data, which considerably reduces costs for governments and industry (see section 1.1 above). In the context of the sound management of chemicals and waste beyond 2020, ways to promote global acceptance of data on chemicals' hazards might be agreed by countries.

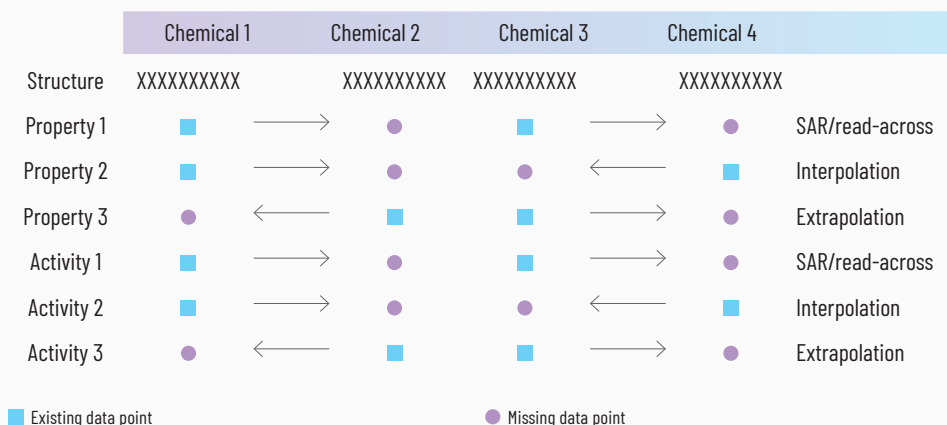
1.3 New approaches are accelerating hazard assessment

Encouraging progress is being made through emerging approaches, e.g. grouping, and read-across

New Approach Methodologies and their integration in regulatory settings are being widely discussed because of their potential to complement traditional approaches (ECHA 2016a; Environment and Climate Change Canada 2016; US EPA 2018e) (see also Part III, Ch. 3). In addition to the growing use of *in vitro* (non-animal) testing methods, *non-testing* methods are increasingly used to obtain data on chemical hazards. This may involve grouping chemicals based on similar properties and then filling data gaps through read-across (Figure 1.2) (Berggren *et al.* 2015). Furthermore, a joint US EPA, Government of Canada and ECHA initiative on Accelerating the Pace of Chemical Risk Assessment (APCRA) aims to develop a series of joint case studies which could help increase the use of New Approach Methodologies for chemical prioritization, screening and quantitative risk assessment (ECHA and US EPA 2016).

ECHA reported in 2017 that read-across was the most common alternative method used by industry to comply with Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) hazard information requirements (ECHA 2017b). Assessments under Canada's Chemicals Management Plan also commonly use read-across (Government of Canada 2017). For grouping challenging substances such as nanomaterials, progress has been made in using read-across (ECHA 2017c).

The development of computer tools such as the OECD's QSAR Toolbox for Grouping Chemicals into Categories (OECD 2007; Dimitrov *et al.* 2016; OECD 2018j) or the European Chemical Industry Council's AMBIT (Jeliaskova *et al.* 2016; European Chemical Industry Council Long-Range Research Initiative 2017) exemplify the trend to use read-across for chemical hazard assessment. The QSAR Toolbox helps users apply read-across by identifying relevant structural characteristics and the potential mechanisms or mode of

Figure 1.2 Graphical representation of a chemical category and some approaches for filling data gaps (adapted from OECD 2014a, p. 14)

In a group of chemicals whose physical-chemical and human health and/or ecotoxicological properties and/or environmental fate properties are likely to be similar, or to follow a regular pattern (usually as a result of structural similarity), not all of these chemicals need to be tested for all properties. Above is a representation of some approaches that can be used to fill data gaps: SAR (structure-activity relationship)/read-across, interpolation and extrapolation.

action of a target chemical. It also helps identify other chemicals that have the same structural characteristics and/or mechanism or mode of action.

A more holistic approach to information generation is needed

Despite the progress already made, a more holistic approach to testing across national jurisdictions could involve defining categories and jointly identifying priority chemicals for testing. The results could be used to inform a better understanding of the properties of many other chemicals in the same category (US EPA 2010; Government of Canada 2016b). Further integration of information generated through toxicity and ecotoxicity testing could also help achieve a more holistic approach to interpreting hazard information.

The OECD's Mutual Acceptance of Data system has been effective in ensuring wider acceptance of test data. However, efforts to bring about the acceptance of conclusions on hazard identification that use different types of information (such as *in silico* or computational data) have not been as successful. One reason could be that regulators are not yet fully convinced of the reliability of the newer methods since insights

into the validity of the results have not yet been accepted internationally. As science advances, growing confidence in these new methods could nurture broader regulatory acceptance. In the context of sound management of chemicals and waste beyond 2020, agreements on international standardization and validation efforts could widen the availability of information on hazard properties and promote wider (if gradual) regulatory acceptance globally, leading to significant efficiencies.

A new hazard assessment paradigm focusing on Adverse Outcome Pathways is being developed

As a possible bridge towards 21st century toxicity testing (see section 1.1 above), the concept of Adverse Outcome Pathways (AOPs) is gaining momentum and is being investigated. An AOP is "a logical sequence of key events triggered by chemical exposure and occurring at the molecular, cellular, organ, whole organism or population level" (OECD 2017). An AOP investigation involves studying an interaction at a molecular target (a Molecular Initiating Event, or MIE), which then signals events within a cell or tissue and leads to an adverse outcome. The adverse outcome can occur at any biological

level of organization. It could have regulatory significance if it corresponds to a protection goal or endpoint in a regulatory guideline test. Interactions among the levels within an AOP may be causal, mechanistic, inferential or correlation-based. By gathering mechanistic information relevant to specific adverse outcomes, regulators might be able to identify key events that are predictive of the adverse outcome, and for which (*in vitro*) test methods can be developed. While experience with the use of AOPs is limited – and there is still a significant gap between AOP-based approaches and hazard assessment that is based on traditional test data – AOPs are already particularly helpful for obtaining in-depth insights into the mechanism of the toxicity exhibited by groups of chemicals.

Information generated through an AOP can be used, for example, to:

- › interpret results from non-standardized test methods;
- › group chemicals into toxicologically meaningful categories;
- › develop testing strategies; or

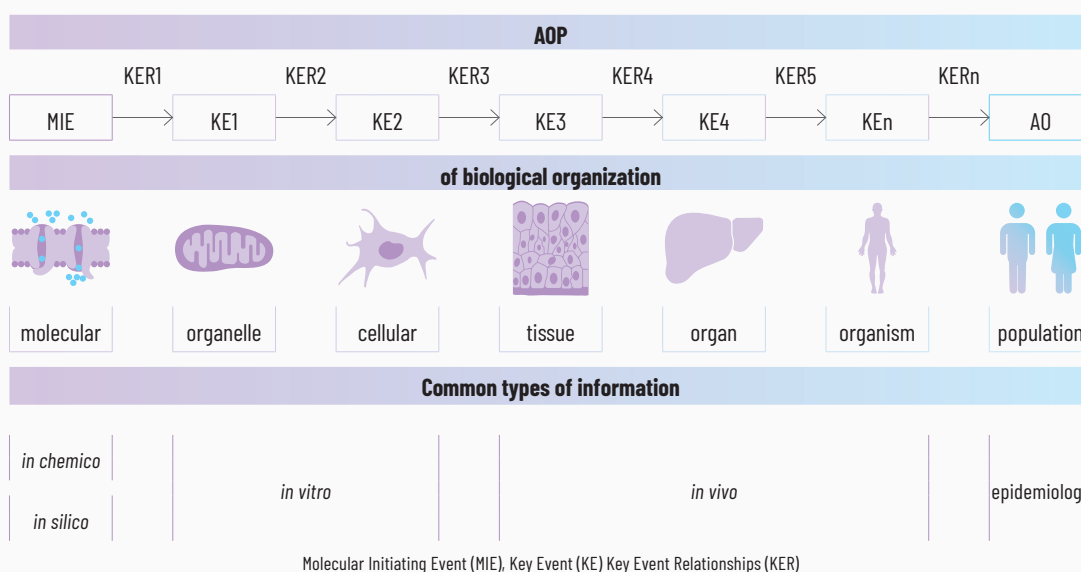
- › select test methods that can be standardized and harmonized.

Figure 1.3 illustrates the AOP concept within an Integrated Approach to Testing and Assessment (IATA). This approach has already been successfully piloted for the hazard endpoint of skin sensitization. OECD Test Guidelines have been developed for all relevant key events in the AOP (OECD 2014b). The success of this approach for other endpoints will depend on the availability of scientific knowledge about the mechanism of action of chemicals. To further strengthen the scientific robustness of predictions based on grouping and read-across, regulatory authorities are using the AOP concept by, for example, grouping chemicals that are predicted to trigger the same AOP. As a single AOP is unlikely to capture all events of potential regulatory significance, AOP networks (based on AOPs that share at least one common element) will help provide further representation of pathways that lead to adverse outcomes (Delrue *et al.* 2016).

Opportunities to accelerate chemical hazard assessment and fill knowledge gaps

Many countries are actively engaged in assessing the hazards and risks of priority chemicals on

Figure 1.3 Testing and assessment based on the Adverse Outcome Pathway (AOP) concept (adapted from Vinken *et al.* 2017, p. 3699)



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their markets, as called for by the 2020 goal (see Part II). Nevertheless, the generation of new and robust test results remains quite limited. The ECHA has reported that, overall, 11 per cent of total REACH information requirements were generated by new experimental studies performed on vertebrate animals (ECHA 2017d). Given that alternative methods are still evolving, authorities are having difficulty assessing the hazards of a number of chemicals, including those that potentially have CMR (carcinogenic, mutagenic or reprotoxic) properties based on such methods.

A study by the German Federal Institute for Risk Assessment found that for chemicals produced in volumes above 1,000 tonnes which were registered under REACH, an average of 39 per cent were compliant with the information requirements for eight toxicological endpoints, ranging from 19 per cent for developmental toxicity to 56 per cent for biotic degradation. The rest of the dossiers were non-compliant or did not allow final conclusions to be made on the dossier due to methodological limitations (ECHA 2017e). Better compliance with information requirements would obviously help accelerate hazard assessments.

The ECHA estimated that of 4,450 substances manufactured or imported above 100 tonnes/year registered under REACH, about 3,000 could not be categorized as either low or high priority for in-depth evaluation, partly due to lack of hazard data, but also partly due to insufficient use information to allow this type

of categorization (ECHA 2016a). In the recently completed registration of existing chemicals in the EU, 5,900 chemicals were registered in the 1-10 tonnes/year range and 4,000 in the 10-100 tonnes/year range. These chemicals still need to be considered by the ECHA.

Limited generation of new test results also has repercussions on the use of grouping and read-across. These techniques rely on the presence of high-quality experimental results for at least some members of a group or category of chemicals. In the absence of adequate experimental results for close analogues, this approach cannot be applied. That may be especially problematic in the case of low-volume production chemicals, for which most jurisdictions do not require test data. In such cases information for classification and labelling may also be derived from non-test methods, as is the case for new chemicals under the Toxic Substances Control Act (TSCA) in the United States (US EPA 2017).

1.4 Achieving globally harmonized classifications of chemicals is challenging, but valuable

Globally harmonized criteria are accepted, but how feasible are globally accepted classifications of chemicals?

The development of the Globally Harmonized System for Classification and Labelling of Chemicals (GHS) and its implementation by a

Table 1.1 Health hazards and environmental hazards – classes for global hazard classification (Derived from UN 2017)

Health hazards	Environmental hazards
<ul style="list-style-type: none"> › Acute toxicity › Skin corrosion/irritation › Serious eye damage/eye irritation › Respiratory or skin sensitization › Germ cell mutagenicity › Carcinogenicity › Reproductive toxicity › Specific target organ toxicity–single exposure › Specific target organism–repeated exposure › Aspiration hazards 	<ul style="list-style-type: none"> › Hazardous to the aquatic environment › Hazardous to the ozone layer

growing number of countries has been one of the successes in the field of chemical safety during the last 20 years (Persson *et al.* 2017; UNECE n.d.). Globally harmonized classification criteria have been developed for physical, health and environmental hazards. Table 1.1 shows the specific health and environmental hazards covered by the GHS (United Nations [UN] 2017). Despite the many hazards covered already, work could be undertaken to increase the number of hazard criteria, particularly with respect to environmental hazards and endocrine disruption.

While the GHS has established harmonized criteria for hazard classification, companies – and, in some cases, governments – classify chemicals individually. This may result in different classifications of the same chemical due to different interpretations of available test results. Not only can different classifications of the same chemical create confusion, but such parallel classifications may waste resources. Although it might be difficult to achieve a globally harmonized list of classified chemicals, work is ongoing to explore the potential development of such a list in a cost-effective manner (OECD 2016).

A pilot classification project has been carried out for three substances, each sponsored by a country or agency (OECD 2016). The sponsors spent an average of 38 days drafting and updating the substance classification proposals. Reviewers then spent another five days checking them. The report from the pilot exercise demonstrated that the process is feasible; however, it would require sustained commitment of time and resources by countries and other interested parties.

In view of the resources needed to develop a global list of chemicals with harmonized classifications, agreement has not yet been reached on whether to begin this initiative. Such a list of classified substances would not only create consistency, but would significantly benefit countries with few resources. In the absence of such a list, the work of the International Labour Organization (ILO) and the WHO to produce International Chemical Safety Cards (ICSC) in line with the GHS is very useful (WHO 2019). To date, more than 1,700 of these cards are available in English, while national institutions translate them

into their respective languages (ILO 2018). In addition, the EU has already agreed on harmonized classifications for chemicals using GHS criteria. These national or regional lists of classified chemicals can be consulted by countries with limited resources which are committed to implementing the GHS.

ACUTE HAZARDS		PREVENTION	FIRE FIGHTING
FIRE & EXPLOSION	Highly flammable. Vapour/air mixtures are explosive. Risk of fire and explosion on contact with incompatible substances. See Chemical Dangers.	NO open flames, NO sparks and NO smoking. Closed system, ventilation, explosion-proof electrical equipment and lighting. Do NOT use compressed air for filling, discharging, or handling. NO contact with incompatible materials. See Chemical Dangers.	Use water spray, powder, alcohol-resistant foam, carbon dioxide. In case of fire, keep drums, etc. cool by spraying with water.
	STRICT HYGIENE! PREVENT GENERATION OF MISTS!		
SYMPTOMS		PREVENTION	FIRST AID
Inhalation	Cough, Headache, Fatigue, Drowsiness.	Use ventilation, local exhaust or breathing protection.	Fresh air, rest.
Skin	Dry skin.	Protective clothing, Apron, Protective gloves.	Remove contaminated clothes. Rinse skin with plenty of water or shower.
Eyes	Redness, Pain, Burning sensation.	Wear safety goggles.	First rinse with plenty of water for several minutes (remove contact lenses if readily available), then refer for medical attention.
Ingestion	Burning sensation, Headache, Confusion, Dizziness, Unconsciousness.	Do not eat, drink, or smoke during work.	Rinse mouth. Give one or two glasses of water to drink. Refer immediately for medical attention.
SPILLAGE DISPOSAL		CLASSIFICATION & LABELLING	
Remove all ignition sources. Ventilation. Do NOT wash away into sewer. Collect leaking and spilled liquid in covered containers as far as possible. Absorb remaining liquid in inert absorbent. Wash away remainder with plenty of water. Store and dispose of according to local regulations.		According to UN GHS Criteria  DANGER	

1.5 Global relevance of the growing knowledge about chemical hazards

Improved knowledge-sharing

Owing to the internet and other information technology, the availability and accessibility of data for use in hazard and risk assessment has greatly improved in the last two decades. A number of portals facilitate locating relevant data (Wexler *et al.* 2016) relevant for classification and labelling, as well as results already obtained and documented in countries and by intergovernmental organizations. While the databases include a wealth of information, users may still need to interpret the data and derive the resulting hazard characterisations and hazard classifications. The eChemPortal (Box 1.1) is an example of a portal featuring full hazard assessments and/or classifications with the underlying data and justifications.

An example of a more specialized portal developed by the ECHA and the OECD is the International Uniform Chemical Information

Box 1.1 The eChemPortal (OECD n.d.)

The eChemPortal (www.echemportal.org) is a global portal providing information on chemical substances. Managed by the OECD, it is an example of the recently developed internet portals that provide easy access to information relevant for chemical safety and regulatory decision-making. eChem allows users to search for information on individual chemicals or to query by property (e.g. chemicals on which a positive test result for carcinogenicity is available). As of 2017, 34 data sources were participating in this initiative and 13 of them had GHS classification information.

The screenshot shows the eChemPortal website. At the top left is the OECD logo. On the right, there are 'Print' and 'English' options. The main header reads 'The Global Portal to Information on Chemical Substances' and 'eChemPortal'. A left-hand navigation menu lists various search and information options. The main content area highlights three search categories: 'Chemical Substance Search' (34 data sources), 'Chemical Property Data Search' (4 data sources), and 'GHS Search' (2 data sources). Below this, it states that eChemPortal provides free public access to chemical information, listing categories like Physical Chemical Properties, Ecotoxicity, Environmental Fate and Behaviour, and Toxicity. A 'Latest news' section on the right lists updates from February 2019 to September 2017. The footer contains copyright information and a 'Home' link.

Database (IUCLID). IUCLID is a software application which allows users to record, store, maintain and exchange data on the intrinsic and hazard properties of chemical substances. It is an important software application for regulatory bodies and the chemical industry, which use it to implement various regulatory programmes (ECHA and OECD 2018). The ECHA

also maintains databases on the safe use of chemicals including nanomaterials ("Search for Chemicals": ECHA n.d. b). These databases combine information submitted by industry with that gathered and generated by the ECHA, competent authorities in EU Member States and other regulators. Information which is (or will be) available from the ECHA is described in Box 1.2.

Box 1.2 The European Chemicals Agency's longer-term vision for improving access to information (ECHA 2016b)

In years to come the European Chemicals Agency (ECHA) will be taking on new tasks, such as establishing a new central database, by the end of 2019, with information available to waste treatment operators and consumers about substances of concern (ECHA 2018). It may also host the European Chemicals Legislation Finder (EUCLEF), bringing together information on European Community legislation regulating chemicals. This will further increase the volume of data held by the ECHA in its databases.

In this context, the ECHA has a long-term vision of increasing and simplifying access to the vast scientific data collections it holds and encouraging the reuse of these data (ECHA 2016b). As part of that effort, it is currently preparing an initiative to explore opportunities for a common data platform, together with the European Food Safety Authority (EFSA) and with the support of the European Parliament. This initiative aims to include a registry of toxicological studies for chemical substances and regulated products performed by industry (which could also be fed by third parties such as academic institutions) in order to serve as an open repository for research and scientific data. Such a platform could provide data analytics, predictive toxicology (which could avoid animal testing), better environmental monitoring, better study design, the development of artificial intelligence, and machine learning applications.

Opportunities for mutual acceptance of hazard assessments

The elaboration of chemical hazard assessments is resource-intensive. While there is a system in place for countries' acceptance of test results generated in other countries, there is currently no agreed international understanding on acceptance of the outcome of a hazard assessment performed in other countries. Such a system could greatly reduce the resources needed by national regulators (e.g. for classification and labelling). Companies and government agencies, especially in countries with limited resources, would benefit from the public availability of these assessments, particularly if they were well-documented (ECHA n.d. c).

The Industrial Chemicals Bill introduced in Australia in 2017 allows regulatory decisions to be taken based on the hazard assessment of a "trusted international body". Hazard assessment schemes in Canada and the EU are listed explicitly, while other bodies could potentially be added (Parliament of the Commonwealth of Australia 2017). The development of internationally harmonized criteria for what constitutes a "trusted international body" or a "trusted body" would increase the reuse of existing assessments. Alternatively, countries that need a hazard assessment (combined with exposure

information) to support national decision-making could use results generated in several other countries if the hazard assessments have similar outcomes. In light of these opportunities, wider acceptance of hazard assessments could be a topic to examine in the context of sound management of chemicals and waste beyond 2020.

1.6 Potential measures to further advance hazard assessment

Harmonized methodologies for mutual acceptance of chemical hazard test data, standardization in regard to accepting test results, and a global list of hazard classifications would result in major efficiencies for all actors concerned. This harmonization would benefit, in particular, countries with limited resources. Taking into account the preceding analysis, stakeholders may wish to consider the following measures to further advance hazard assessment:

- › Accelerate the generation of more comprehensive information about the intrinsic hazards and properties of chemical substances and make this information publicly available.

- › Continue to work towards achieving wider international acceptance of chemical hazard test data, particularly with a view to animal welfare.
- › Continue to work towards global agreement on standardization and validation efforts in regard to accepting chemical hazard data estimation results, as well as with a view to animal welfare.
- › Further explore new approaches to fill data gaps and scale up the use of portals to facilitate the availability and accessibility of hazard data.
- › Accelerate development of the concept of Adverse Outcome Pathways (AOPs) to support hazard assessment.
- › Develop new GHS criteria (e.g. for further environmental hazards, endocrine disruption).
- › Continue to explore possibilities to develop a globally harmonized list of classified chemicals based on the GHS hazard classification criteria.

2/ Exposure assessment: benefiting from internationally available resources

Chapter Highlights

Modelling-based approaches have greatly enhanced knowledge about the distribution of chemicals in the environment and exposure situations.

National, regional and other contexts can play a role in determining levels of exposure.

Exposure scenarios and models are available for a range of situations. They can provide a generic basis for human and environmental exposure assessments, thus saving resources.

Wider awareness of available generic exposure assessment methods and models will help obtain insights into local human and environmental chemical exposure.

Advances are being made with respect to methods to quantify exposures from products. However, more data on product ingredients and more research are needed in this field.

Further work is needed to elucidate aggregate exposures to the same chemical, across sources, and cumulative exposures across chemicals.

Exposure assessment is context-specific, yet it may benefit from work done in other contexts or countries. This chapter summarizes state-of-the-art knowledge, methods and resources relevant for determining levels of exposure of humans and environmental media. While the national and regional specificities of the exposure context are recognized, generic exposure scenarios which could be useful in exposure assessment are highlighted. These scenarios may be particularly useful in countries that have limited resources to devote to chemicals management.

2.1 Understanding exposure to chemicals has greatly improved

Exposure of workers, consumers and the environment

Exposure to chemicals takes place in many situations. It may occur through food consumption, product use, uptakes indoors and outdoors, and at the workplace. The magnitude, frequency and duration of exposure to a chemical – or to several chemicals – can be measured or estimated, along with the number and characteristics of the individuals or population exposed. For certain categories of chemicals (e.g. pharmaceutical active ingredients, food additives, cosmetics, and pesticides, including biocides) the doses recommended to be applied in their normal use are often determined and known in advance. Therefore, the assessment

information available is usually more precise than for industrial chemicals. In the case of a pesticide active ingredient, for example, it is possible to examine the frequency, timing and levels of contact of workers under particular conditions of use, assuming that recommended practices are followed (US EPA 2017a). In the case of industrial chemicals and chemicals in products, lack of information on actual uses may impede drawing conclusions about the assessment of priorities and risks.

Ideally, an exposure assessment should describe sources, routes, pathways, and the uncertainty in the assessment (WHO 2004). In the assessment of human exposure many different aspects require specific consideration: the exposure route (inhalation, ingestion, dermal); the subjects of exposure (workers, the general population/consumers, including vulnerable groups, and ecosystems); and the media which can give rise to exposure (air, water and sediment, soil and dust, food aquatic biota, consumer products).

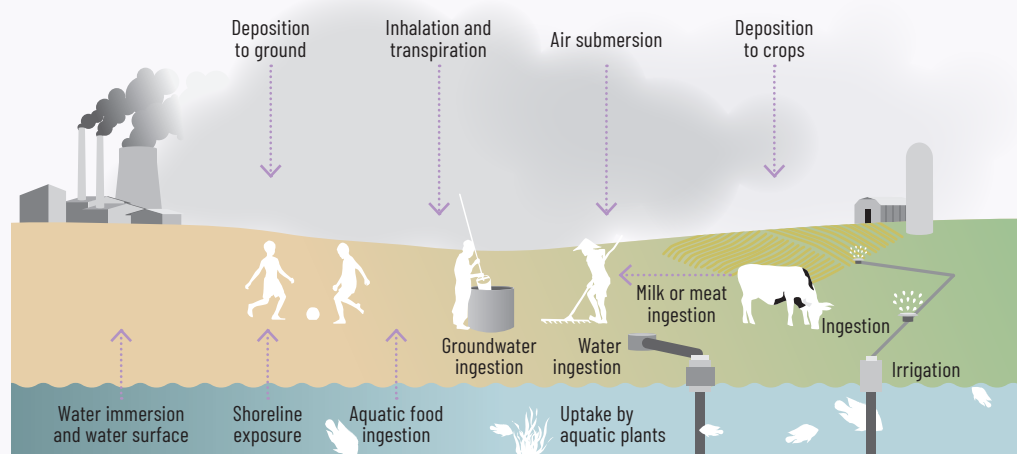
Exposure can also occur through a combination of routes and media. The figure in Box 2.1 shows human exposure to chemicals through

different environmental pathways. Besides exposure via environmental pathways, the human population can be exposed through products and indoor air emissions. In exposure assessments special attention needs to be paid to vulnerable categories such as foetuses; infants and children; women of childbearing age; pregnant and lactating women; and older adults (US EPA 2017a). The specific method used to measure or estimate exposure will depend on factors such as the purpose of the assessment and the quality and quantity of the data required (US EPA 2017b). Exposure assessments will not necessarily be relevant in all other countries or contexts. For example, conditions of pesticide use differ between and within countries.

Measurement-based approaches are valuable, but not always possible

Measuring and monitoring the presence of a chemical in humans (human biomonitoring) or in environmental media (environmental monitoring) is one way to determine levels of exposure. Environmental monitoring is usually carried out to define the current state of the environment (e.g. when a problem related to a

Box 2.1 Human exposure to chemicals – environmental pathways (adapted from Faustman and Omenn 2013, p. 138)



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In environmental exposure assessment, concentrations in water, sediment, soil and air are often determined (measured or calculated) in order to obtain insights into exposures of environmental species. Photodegradation, biodegradation and bioaccumulation are important factors that should also be taken into consideration. Geographic variability caused by differences in abiotic conditions such as climate, hydrology, geology and biotic conditions (e.g. differences in ecosystem structures and functions) can also influence the outcomes of environmental exposure assessments.

specific chemical is suspected) and/or to establish trends in environmental concentrations (e.g. to measure compliance with restrictions imposed on releases).

In order to determine environmental exposure, many methods exist to measure concentrations in air, water, soil and solid waste (US EPA 2017c). Such chemical analyses are usually carried out on samples taken at specific locations and times. The measured concentrations can therefore reflect variations in space and time. Measurements always need to be considered in the context of knowledge about the process leading to exposure, which could mean complicated and resource-intensive follow-up to obtain additional information. Nevertheless, provided the monitoring conditions are well-documented, information obtained through monitoring programmes can be helpful in making environmental exposure assessments (OECD 2013).

Biomonitoring is a method by which concentrations of naturally occurring and

synthetic chemicals are measured in body fluids (e.g. blood, urine and breast milk) or tissue (e.g. hair, nails, fat and bone) (Box 2.2). This allows identification of the extent to which certain chemicals have entered the body and, in the case of regular measurements, how exposure may change over time. Methods that use pooled blood and urine samples to identify the most prevalent chemicals of concern in sub-populations at risk, such as children, also exist. Combining multiple individual specimens into a single sample can be a cost-effective way to monitor exposures and trends and to identify highly exposed sub-populations (Aylward *et al.* 2014; Heffernan *et al.* 2014; Heffernan *et al.* 2015). Biomonitoring can therefore provide precise information on the total internal exposure of an individual at a given time, as it adds together exposure from multiple sources and routes (e.g. air, water, food), thus also providing information on inter-individual variability and vulnerability.

In the occupational setting, according to the ILO Code of Practice, employers should monitor and

Box 2.2 Programmes to monitor chemicals in humans and the environment

A number of biomonitoring programmes exist. In the United States, the National Health and Nutrition Examination Survey (NHANES) is a survey research programme which aims to assess the health and nutritional status of adults and children in that country and track changes over time (United States Centers for Disease Control and Prevention [US CDC] 2018a). Much information on human exposure to environmental contaminants in the United States is made available by the Centers for Disease Control and Prevention (US CDC 2018b). As part of the Canadian Health Measures Survey (CHMS), levels of certain chemicals in the blood and urine of the population are measured (Government of Canada 2018). In the EU the Human Biomonitoring for Europe (HBM4EU) programme coordinates, advances and harmonizes human biomonitoring in Europe (Becker *et al.* 2014). This programme is expected to provide better evidence of the actual exposure of citizens to chemicals, and possible health effects, than is currently available, with a view to support policymaking (HBM4EU 2018).

The European Commission's Information Platform for Chemical Monitoring (IPChem) is a reference access point for searching, accessing and retrieving chemical occurrence data collected and managed in Europe. It has been developed to fill the knowledge gap on chemical exposure and its burden on health and the environment. IPChem is structured into four modules, according to the chemical monitoring data categorization: Environmental Monitoring, Human Bio-Monitoring, Food and Feed, and Products and Indoor Air (EC 2018). In addition, scientists and stakeholders from 35 institutions in 27 European countries are working within a human biomonitoring framework, the Consortium to Perform Human Biomonitoring on a European Scale (COPHES) (COPHES 2016).

The Stockholm Convention has put in place sustainable, harmonized and comparable human biomonitoring activities through collaboration with the United Nations Environment Programme (UNEP) and the WHO. A report on the results of a global survey on concentrations in human milk of persistent organic pollutants (POPs) was published in 2013 (UNEP and WHO 2013 and is being updated to include newly listed POPs.).

record the exposure of workers to hazardous chemicals to ensure their health and safety (ILO 1993; ILO 2004). They should also ensure that workers are not exposed to chemicals to an extent that exceeds exposure limits or other exposure criteria for the evaluation and control of the working environment. Based on monitoring data, employers should assess workers' exposure to hazardous chemicals and provide these data to the workers. These ILO requirements have been implemented in many countries (ILO 2011). This means many countries will have information about levels of exposure to a number of chemicals for a variety of occupations. The outcomes of these measurements of exposure can be of use in carrying out more generic exposure assessments.

Measurements-based approaches may be used to assess occupational exposures to chemicals throughout the supply chain of products. Such research reveals that the main exposures may occur at the intermediary stages of product manufacturing (Kijko *et al.* 2015; Kijko, Jolliet and Margni 2016). For example, in a study on occupational exposure associated with an office lounge seat, the greatest occupational exposure occurred during production of the plastic materials and resin, rather than during manufacturing of the seat or in the chemical industry (Kijko, Jolliet and Margni 2016).

Representative and reliable monitoring data are available for only a small number of industrial chemicals. Lack of measured data therefore does not mean there is a lack of exposure. Alternatively, exposure modelling and release estimation methods are widely used to obtain insights into exposure scenarios. Work process-based approaches consider potential impacts on worker health as a ratio of reported work-related morbidity and mortality to the output of industrial processes (Scanlon *et al.* 2015). In using these methods, it needs to be acknowledged that the conditions of use of a chemical can be vastly different and can be more dangerous in developing countries than in developed ones, while developing countries usually lack the resources to carry out full exposure assessments.

National and regional specificities need to be recognized

While hazard is an intrinsic property of a chemical, exposure varies widely according to, for example, process conditions, the formulation of the product used and socio-economic conditions. With respect to environmental exposure, local aspects such as climate, average temperatures or water conditions can be significant. Given the variety of specific situations, conditions and/or purposes for which exposure assessments



may be carried out, the results of exposure assessments cannot be directly translated from one country or region to another. If conditions are similar, however, exposure scenarios produced in some countries may provide generic insights for the conduct of exposure assessments in similar contexts.

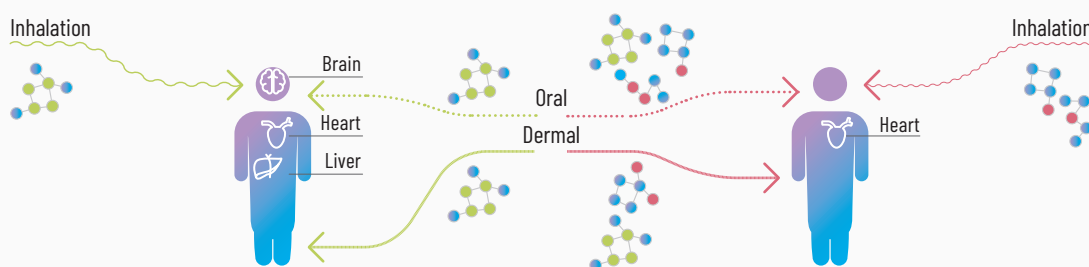
One tool for obtaining valuable information on local emissions of selected chemicals is a Pollutant Release and Transfer Register (PRTR). Under PRTR systems, point source emitters such as industrial facilities are required to report the quantities of chemical releases. These are then made available in publicly accessible databases or inventories. Emissions can be measured or estimated with the help of a wide array of available techniques (e.g. use of emission factors). Such information, in combination with effects indications, can help identify possible exposures and risks. Companies also use PRTR data to identify opportunities to improve efficiencies and reduce waste (OECD 2018a; UNECE 2018; United Nations Institute for Training and Research [UNITAR] 2018). Some PRTRs cover non-point or diffuse sources (e.g. mobile sources). The possibility of including chemical releases from products has been studied, and these releases are included to a certain extent in some countries (Nordic Council of Ministers 2006; OECD 2017).

Understanding aggregate and cumulative exposure to chemicals is challenging

In daily life humans are rarely exposed to a single pollutant from a single source. Instead, they are exposed to a multitude of distinct organic and inorganic chemical substances found in indoor and outdoor environments (UNEP 2017; Gligorovski and Abbatt 2018). Each of these substances is associated with a variety of sources along product life cycles and following various exposure pathways, including those that contribute to inhalation, ingestion and dermal exposures. Likewise, ecosystems around the world are exposed to releases of numerous industrial and agricultural chemicals, either intentionally (e.g. pesticides) or unintentionally (e.g. pharmaceuticals). The cumulative exposure of ecosystems to the mixture of chemicals entering the environment has been identified as one of the five main pressures negatively affecting biodiversity (Secretariat of the Convention on Biological Diversity 2010). How this chemical “cocktail” interferes with human health, and how it interacts with organisms and the environment, is still largely unknown.

Single-chemical assessments may fail to adequately account for potential synergistic or antagonistic effects of chemical mixtures in humans and ecosystems. Aggregate exposure

Figure 2.1 Aggregate (left) and cumulative (right) exposure (adapted from US EPA 2017d)



Aggregate exposure assessment considers combined exposures to a single stressor across multiple routes and multiple pathways. Cumulative exposure assessment generally evaluates combined exposure to multiple stressors via multiple exposure pathways that affect a single biological target.

across sources for the same chemical and cumulative exposure across chemicals (Figure 2.1) are therefore receiving increasing attention, along with the assessment of associated risks. Efforts to address the combined effect of chemical mixtures, such as multi-substance effect indicators for freshwater ecosystems (Posthuma *et al.* 2016), are under way. However, scientists are just beginning to derive principles that allow broader consideration of cumulative exposures and related mixture toxicity effects in humans and ecosystems (Altenburger *et al.* 2013).

To advance aggregate and cumulative exposure assessment, a number of research advances need to be made. First, systematic production and use of high-throughput exposure data (Cohen Hubal *et al.* 2010; Wambaugh *et al.* 2013) are required in order to feed complex exposure models. Second, consistent and mass balance-based integration of exposure pathways and indoor-outdoor environments in frameworks based on strictly comparative metrics is essential to systematically identify exposure hotspots and focus higher-tier assessments (Fantke *et al.* 2016). Third, mechanisms are required that support the integration of global data and tools to foster our understanding of the complexity of exposure through exposome research, which takes into account exposure to exogenous chemicals as well as endogenous chemicals that may be affected as a consequence of exogenous influences (Escher *et al.* 2017). Finally, better linking of exposure outcomes to multi-stressor toxicity information is needed to capture important correlations between chemicals, pathways and effects.

2.2 How can exposure be better quantified?

A stepwise process to cover exposure throughout the life cycle

To better quantify the totality of exposures, especially when resources are limited, it is useful to focus on several steps in the assessment process:

- › Obtain information about the different uses, and quantities thereof, within different regulatory contexts.
- › Define chemical usage scenarios and the masses emitted during manufacturing (that is, at the workplace) and other life cycle stages.
- › Identify the fate and exposure processes that result in transfers to biota and to humans.
- › Determine exposure to the chemicals in consumer products.

Use of generic exposure scenarios is valuable for industrial chemicals

It is not always necessary to carry out resource-intensive measurements to obtain insights into exposure levels. To help countries with limited resources derive such insights, valuable information is available for understanding exposure scenarios. An exposure scenario has been defined as “a combination of facts, assumptions, and interferences that define a discrete situation where potential exposures may occur. These may include the source, the exposed population, the time frame of exposure, microenvironment(s), and the activities. Scenarios are often created to aid exposure assessors in estimating exposure” (WHO 2004). In the EU’s REACH Regulation an exposure scenario refers to an identified use, or group of similar identified uses, such as formulation, processing or production of an article (ECHA 2016). In the United States, EPA generic scenarios and emission scenarios are built into the ChemSTEER tool, with ExpoCast allowing exposure estimates to be made (US EPA 2016; US EPA 2018).

Emission scenario tools available to assess exposure

Predicting emissions of chemicals from specific industrial processes, or from uses for the purpose of exposure assessment, can be uncertain. To help address this challenge, the OECD has developed Emission Scenario Documents (ESDs) that describe the sources, production processes, pathways and use patterns

Box 2.3 OECD Emission Scenario Documents (ESDs) (OECD 2018b)

Emission Scenario Documents (ESDs) aim to quantify the emissions of a chemical into water, air, soil and/or solid waste. An ideal ESD should include the following stages:

1. production
2. formulation
3. industrial use
4. professional use
5. private and consumer use
6. service life of product/article
7. recovery
8. waste disposal (incineration, landfill)

of (groups of) chemicals (Box 2.3). ESDs also offer the possibility of obtaining well-supported estimates of exposure. These estimates can be used as default values in the assessment process unless more specific information on the use and release of a chemical becomes available (e.g. through industry data or as a result of further research). Wider use of the ESDs concept could be considered in the context of the sound management of chemicals and waste beyond 2020, as a potential tool to assist countries with limited resources to estimate exposure.

In the development of the ESDs, 54 use categories and 16 industrial processes have been applied. ESDs aim to quantify, for the specific steps in the life cycle, the emissions of a chemical into water, air, soil and/or solid waste based on available

information or modelling results. They also cover the general mechanisms of diffuse emissions, the accumulation of long-life articles in society, and the relationship between the service life and the other stages in the life cycle chain (OECD 2008; OECD 2018b).

Guidance is available on the generic use of exposure scenarios to better quantify exposures (ECHA 2016). The main users of ESDs are expected to be those who need to estimate emissions of chemicals to the environment during production, use and disposal. This includes regulatory agencies, chemical producers assessing the potential impact of current and new products, and potential users of chemicals who are comparing alternatives. ESDs may also be used in developing estimates of releases for



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PRTRs. ESDs and similar tools, including a number of generic scenarios developed by the US EPA (US EPA 2017e), have been widely used in national and regional contexts (ECHA 2016; ECHA 2018a).

Computer modelling can help inform human and environmental exposure assessment

Insights into exposure levels can be obtained through the use of computer models. Modelling helps to improve the understanding of natural systems and how they react to changing conditions (e.g. exposure to hazardous substances, and the temporal and dose effects from the exposure) (US EPA 2017c). Models are used in risk assessment and risk management to describe the relationship between emissions and concentrations and to predict the outcome of management measures. An advantage of using models is that they allow the evaluation of results of many processes that occur simultaneously, which would otherwise be very difficult (van de Meent and de Bruijn 2007). Models may therefore be valuable for regulatory decision-making and the development of policies. Wider use of models to replace costly analytical monitoring programmes where appropriate – especially in countries with limited resources – could be promoted through training and broader capacity development support projects. There are also models for very specific purposes, such as estimating the overall persistence (Pov) and long-range transport potential of organic chemicals at a screening level (OECD 2018c).

Computer models are available for a number of parameters relevant to exposure assessment. Modelling categories include mass balance modelling; modelling that estimates concentrations and dispersion in environmental media; and multimedia modelling that provides information about the distribution and transport of released chemicals in environmental media. The OECD has made available an overview of 21 modelling categories, which include 56 specific models used in human and environmental exposure assessment (OECD 2012).

Many models are undergoing continuous improvement and refinement over time. The evolution of models covers, for example: different spatial and temporal scales; refined estimation of chemical properties and emission data; incorporation of additional environmental media and processes; and integration of sensitivity and uncertainty analysis in the simulations (Di Guardo *et al.* 2018; ECHA 2018b). For methodologically challenging substances, first generation models are now available to screen for exposure which take into account parameters that are relevant, notably, to nanomaterials (e.g. dissolution, agglomeration, transformation) (Meesters *et al.* 2014).

Such models enable the determination of ecosystem exposure and the prediction of environmental concentrations in freshwater, marine or terrestrial environments for ecological risk assessment. Wannaz *et al.* (2018) used a model predicting the differentiation in freshwater concentrations of a chemical (in this case triclosan [TCS], an antibacterial and antifungal agent used in consumer products) across an entire continent.

Several fate and exposure models allow the determination of human intake fractions via multiple exposure routes and pathways (e.g. inhalation, ingestion of drinking water, fish, meat, dairy products, above and below ground produce, dermal uptake). An example is USEtox, the consensus United Nations Environment Programme-Society of Environmental Toxicology and Chemistry (SETAC) toxicity model (Rosenbaum *et al.* 2008; Rosenbaum *et al.* 2011).

The combination of stochastic prediction of chemical content and product usage with exposure models makes it possible to compare model estimates of internal doses with the biomonitoring data that are becoming increasingly available at population level (Wambaugh *et al.* 2013; Csiszar *et al.* 2017). The external concentration or dose can then be compared with an external No Observed Adverse Effects Level (NOAEL) (see Part III, Chapter 4) or No Observed Adverse Effect Concentration (NOAEC) determined from animal studies.

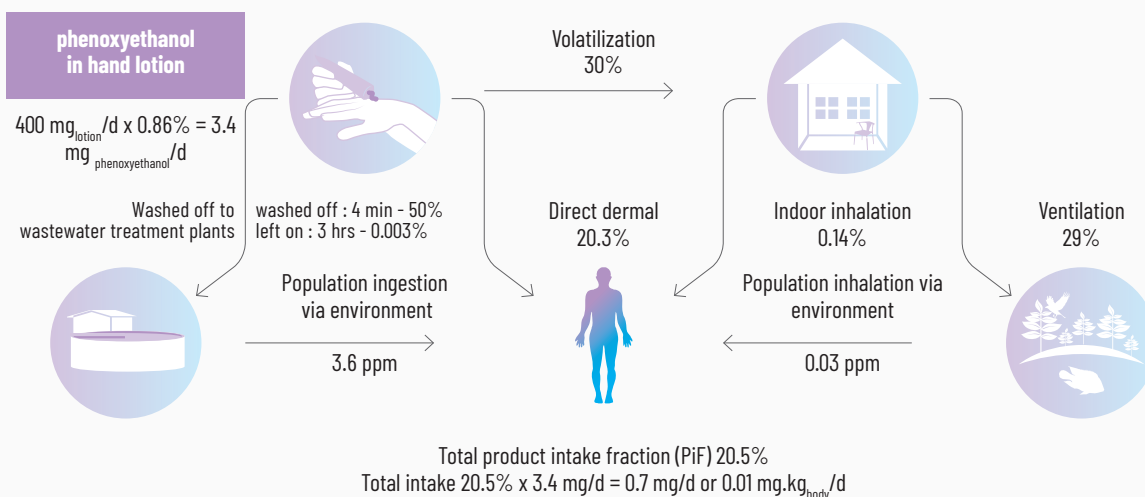
Estimating exposure from products is challenging because of data gaps

To quantify exposure to chemicals in products, the first step is to assess the chemical masses that enter the consumer near-field environment where products are located. Chemical composition and content have been relatively well-characterized for certain classes of products (e.g. for personal care and for cleaning). They are available in various databases (Goldsmith *et al.* 2014) or can be estimated based on chemical function (Isaacs *et al.* 2016). For other products such as articles or building materials, the composition is often unknown. Much wider disclosure of the chemical composition of products is needed in

these cases, even though some databases that are based on product composition declarations exist. An example is the Pharos building materials database (Pharos 2018) (see Part I, Ch. 4 for other examples).

Chemical and product usage also depends on consumer behaviour. To characterize consumer behaviour, combined with the occurrence of chemicals in and releases from products, modelling of product and chemical usage is carried out at the population level. To cover these parameters, stochastic databases have been developed and applied that differentiate between average population and given population groups such as children or high-end users (Isaacs *et al.*

Figure 2.2 Transfer fractions to near-field and far-field compartments and the corresponding product intake fraction for phenoxyethanol used as a preservative at a concentration of 0.86 per cent in a hand lotion (based on from Fantke *et al.* 2016)



Note: All percentages refer to the amount of phenoxyethanol applied.

The Figure indicates the different transfer fractions to near-field and far-field compartments and the corresponding product intake fraction for phenoxyethanol used as a preservative at a concentration of 0.86 per cent in a hand lotion. The 3.4 milligrams (mg) of phenoxyethanol applied on the hand is first transferred to an outer layer of the user's skin (epidermis) (20 per cent), to indoor air (30 per cent) and to the wastewater treatment plant (50 per cent if the lotion is washed off after four minutes, but only 0.03 per cent if is kept on for three hours). For this chemical the resulting total product intake fraction of 20.5 per cent takes place primarily via dermal uptake (20.3 per cent) through the outmost layer of the user's skin (the stratum corneum), with limited user inhalation of 0.14 per cent and negligible population ingestion and inhalation of less than 4 parts per million (ppm), resulting in an intake dose of 0.01 mg/kilogram body/day. Such high-throughput product intake fractions (PIFs) are available for more than 500 chemical ingredients in personal care products, with the PIFs varying from 0.001 per cent to 100 per cent depending on chemical properties (Csiszar *et al.* 2016), and for more than 8,000 chemical exposures in various products (Shin *et al.* 2015; Ring *et al.* 2018).

2014). Once the composition of products is better known, databases and high-throughput modelling tools are better suited to determine chemical releases from the product to the indoor environment. Based on this, it is possible to determine the product intake fraction (e.g. for personal care products, cleaning products, chemicals in articles and building materials, or food contact materials) (Isaacs *et al.* 2014; Fantke *et al.* 2016; Netherlands National Institute for Public Health and the Environment 2018). Chemicals released from products also undergo transport processes in the near-field before being transferred to the natural environment. It is therefore important to consistently combine near-field pathways (indoors and close-to-human environment) and far-field pathways (ambient air, soil, water environment). An example of the outcomes of a predicted intake fraction calculation is presented in Figure 2.2.

The life cycle of a given chemical or product may involve hundreds of different chemicals in its manufacturing. To address this complexity, the “environmental genome of industrial products” has been developed (Overcash 2016). This database for 1,600 industrial chemical products already contains manufacturing energy, process mass intensity, multimedia emissions, modular unit process flow diagrams, and by-products. This information makes it possible to assess and optimize the environmental performance of chemical manufacturing, while minimizing efforts to enter a new chemical due to its modular structure. Industry has also developed a programme which can be used on a voluntary basis by companies to carry out human and environmental risk assessments of ingredients in household cleaning products. In this programme exposure models are developed based on data and extrapolations which can provide useful information for this kind of assessments (Human and Environmental Risk Assessment n.d.).

2.3 Potential measures to further advance exposure assessment

Global action can be taken to promote wider awareness of available generic exposure assessment methods and models, so that all countries could use them to obtain insights into local human and environmental chemical exposure, keeping in mind that the conditions of use of chemicals differ between countries. Taking into account the preceding analysis, stakeholders may wish to consider the following measures to further advance exposure assessment:

- › Compile exposure assessment methods in order to allow a better overview of existing tools.
- › Scale up the estimation of chemical emissions and releases, as well as environmental and human (bio)monitoring programmes, to provide additional information for exposure assessments.
- › Facilitate wider use of, and access to, generic exposure assessment methods and computer models, including through capacity development.
- › Continue developing methods to determine releases from – and exposure to – chemicals in products.
- › Continue developing methods to determine aggregate exposure across sources for the same chemical, and cumulative exposure across chemicals.
- › Make additional efforts to increase transparency about the determination of parameters in chemical exposure models.

3/ Risk assessment: opportunities to improve and accelerate progress

Chapter Highlights

—
New approaches to risk assessment take into account new hazard assessment and exposure assessment methods.

—
Regulatory frameworks are being strengthened in several countries to address emerging challenges in risk assessment, as well as to incorporate new data and approaches.

—
Large amounts of empirical data relevant for risk assessment have been generated and increasingly disseminated publicly.

—
A framework for assessing combined exposures to multiple chemicals is being further developed.

—
The use of screening-level, generic risk-based approaches and grouping of chemicals which are less complicated, and less resource intensive, is advancing.

—
Toolkits to assist in the risk assessment process have been developed for human health risks (WHO) and environmental risks (OECD).

Chemical risk assessments provide decision-makers with predictive analysis concerning the human and environmental health impacts of exposure to chemicals. Important building blocks for the risk assessment process were described in Part III, Ch. 1 (hazard assessment) and Ch. 2 (exposure assessment). This chapter features a broader discussion of risk assessment methods. Opportunities are identified for future work, based on lessons learned. Attention is also drawn to the wealth of relevant publications and services available from national governments and intergovernmental organizations.

3.1 The development of approaches to risk assessment is moving forward

Different forms of risk assessment

Risk assessment can be undertaken from two different perspectives. A chemical-oriented, prospective risk assessment mainly aims to define conditions for the safe use of chemicals. An environmental media-oriented, retrospective risk assessment is intended either to assess the chemical load that is acceptable for a predefined compartment (e.g. a particular river or a human [sub] population). This approach also looks at whether – and to what extent – chemicals contribute to observed adverse human health or environmental impacts. In both cases risks to human health and the environment are considered. With respect to human health, assessments carried out by authorities often

distinguish between risks to workers, consumers (from many different types of products) and the general population.

Risk assessments may take a number of different forms, depending on the particular risk management problem being addressed. Chiu (2017) identified the following levels of risk assessment, which have increasing levels of complexity:

- › Screening and/or prioritization assessments identify potential areas for further consideration or analysis.
- › Safety assessments determine whether existing or proposed exposure levels are “acceptable”.
- › Population-level assessments evaluate the impact of one or more risk management options on an overall population.

In conducting risk assessments, reliable data and proven methodologies are needed. Uncertainties may derive, for example, from lack of adequate

data for dose/response calculations. They may also occur in extrapolating from animal test data to humans and across species, or in determining exposures across life cycles. Moreover, information relevant to assessing the special risks to vulnerable populations is often missing. These data gaps and uncertainties limit how the outcomes of risk assessments can be used in risk management.

Strengthening regulatory frameworks to accelerate risk assessment

Criticism of chemical risk assessment approaches used in the past includes the fact that conducting them is resource-intensive, and that only a limited number of chemicals have been assessed for the risks they pose. Several major regulatory frameworks have therefore been adapted with the objective of facilitating the risk assessment of more chemicals within shorter periods of time. Adaptions also cover new areas such as the possible risks of nanomaterials (Laux *et al.* 2018). A specific framework for assessing manufactured nanomaterials has been put in place under REACH (Gottardo *et al.* 2017; EC 2018a), while the



US EPA is pursuing a comprehensive regulatory approach under TSCA to address nanoscale materials (US EPA 2017).

The amendment of TSCA by the Lautenberg Act of 2016 introduced a clear distinction between risk assessment and risk management (United States Congress 2016). It also mandated risk assessment for vulnerable populations and required that priority chemicals currently on the market (existing chemicals) be explicitly evaluated by the US EPA. For new chemicals, an affirmative safety finding by the EPA is required prior to market introduction. Current discussions revolve around implementation of the amended TSCA (American Chemistry Council 2018; Franklin 2018). In Canada a recent parliamentary review of the Canadian Environmental Protection Act of 1999 resulted in numerous recommendations related to risk assessment, including on vulnerable populations, endocrine-disrupting chemicals, cumulative risk assessment and priority-setting. These recommendations inform ongoing engagement with stakeholders

to determine the future direction of chemicals management in Canada (Box 3.1).

In the EU, REACH has been subject to a recent major review. Although the review concluded, in principle, that REACH is fit for purpose, several shortcomings were identified and measures for improvement were suggested. The issues identified by the European Commission as most urgent were the non-compliance of many of the registration dossiers submitted by industry, and lack of updating of the data that form the basis for risk assessment. Further issues included the need to simplify the authorization process and to ensure a level playing field with non-EU companies (EC 2018b; EC 2018c).

Improving empirical knowledge

Efforts have been undertaken to better organize and systematize empirical knowledge for chemical risk assessment, as well as to increase the availability of exposure, hazard and risk data to regulatory authorities, the public and other stakeholders. New Approach Methodologies

Box 3.1 Canada's Chemicals Management Plan

The Canadian Chemicals Management Plan was launched in 2006 with the aim of reducing the risks posed by chemical substances to human health and the environment (Government of Canada 2016a). As of July 2018, over 80 per cent of the 4,300 substances identified in 2006 – during the categorization process – had been assessed. The remaining substances are expected to be addressed by 2021 (Government of Canada 2018a).

The Chemicals Management Plan Risk Assessment Toolbox offers a range of approaches to address the remaining substances (or groups) effectively by selecting an appropriate and fit-for-purpose approach in each case (Government of Canada 2016b). This ensures that efforts focus on the substances of highest concern and that stakeholders are engaged as efficiently as possible. Canada has also developed the Identification of Risk Assessment Priorities (IRAP) process, which seeks to integrate new information from a wider range of sources to track emerging issues and identify and prioritize substances that require further work (Government of Canada 2017a).

With the conclusion of the current Chemicals Management Plan nearing, Canada will be looking at new directions and objectives for chemicals management after 2020. It will also work on improving the Canadian Environmental Protection Act, 1999, which is the country's framework law on pollution prevention and toxic chemicals (Government of Canada 2018b).

are beginning to be applied in risk assessment, as illustrated by a number of case studies (Shah and Greene 2014; Karmaus *et al.* 2016; Pham *et al.* 2016). Important progress has been made in developing the concept of Adverse Outcome Pathways (AOPs) (Carusi *et al.* 2018) (see also Part III, Ch. 3) and in research on Aggregated Exposure Pathways (AEPs) (Teeguarden *et al.* 2016). Research is also advancing on the human exposome, a concept which includes examining the effects of exogenous chemicals and endogenous chemicals produced (or altered) in response to external stressors (Pleil 2015; Human Exposome Project 2019; EC 2015). Studies are exploring “if mechanistic understanding of the causal links between exposure and adverse effects on human health and the environment can be improved by integrating the exposome approach with the [AOP] concept” (Escher *et al.* 2017). For exposure-driven risk assessments of chemicals, however, more information on exposure patterns would be useful.

High-throughput screening generates hazard data relevant to risk assessments for thousands of chemicals. An example of work being carried out in this field is the US EPA's ToxCast programme, which includes publicly available high-throughput toxicity data on a large number of chemicals (US EPA 2018a). The further development and use of AOPs is important in understanding the mechanisms of toxicity for groups of chemicals. High-throughput screening is particularly useful in priority-setting. While these are all important steps with respect to limiting the use of test animals, in coming years much of the information needed to determine the (long-term) risk challenges of chemicals will still need to be derived through animal testing (ECHA 2017).

Ongoing activities result in large collections of empirical data, which are increasingly being made publicly available. Major data repositories that contain data on hazardous properties and classification, and inform risk assessment, include the US EPA's ChemView (US EPA 2018b), its CompTox Chemistry Dashboard (Williams *et al.* 2017; US EPA 2018c), REACH registration data at ECHA (ECHA n.d. a) and the OECD's eChemPortal (OECD n.d.). Data repositories on chemical

occurrences and exposure are comparatively limited. Recent efforts include the IPCHEM portal of the European Commission (EC 2018d) and the NHANES human biomonitoring data from the National Health and Nutrition Examination Survey of the Centers for Disease Control and Prevention in the United States (US CDC 2018).

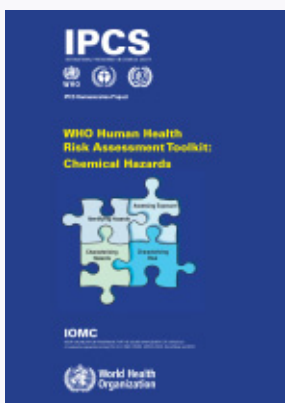
Over the last decade several large-scale programmes have been initiated in the United States and internationally to incorporate advances in molecular and cellular biology, -omics technologies, analytical methods, bioinformatics, and computational tools and methods in the field of toxicology. As noted in the report *Using 21st Century Science to Improve Risk-Related Evaluations* (United States National Academies of Sciences, Engineering and Medicine [US NASEM] 2017), “similar efforts are being pursued in the field of exposure science with the goals of: obtaining more accurate and complete exposure data on individuals and populations for thousands of chemicals over the lifespan; predicting exposures from use data and chemical-property information; and translating exposures between test systems and humans”.

These efforts, separately and combined, help enlarge the knowledge base for risk assessment. However, they focus mainly on improving the empirical knowledge base for human health-oriented risk assessments. Improving the knowledge base for environmental risk assessments has received comparatively little attention – leading, for example, to a call to establish landscape-level monitoring of pesticide impacts (pesticidovigilance) (Milner and Boyd 2017). Moreover, such initiatives are currently mainly restricted to a small number of countries which already have significant experience in the field. Countries with limited resources for risk assessment often do not have widely available data repositories (Wang *et al.* 2015).

International support to assist countries with risk assessments

A number of resources are available from international organizations to provide assistance with chemical risk assessments. The WHO, for example has developed a Human Health Risk

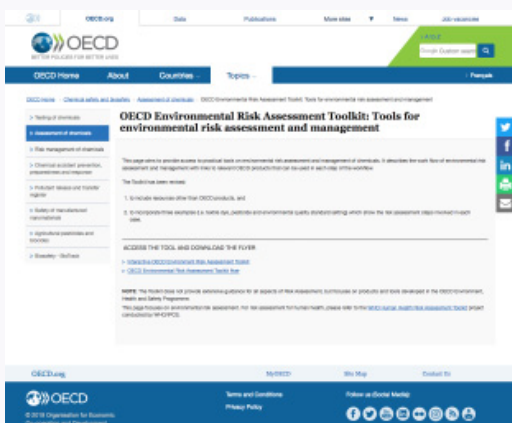
Box 3.2 The WHO Human Health Risk Assessment Toolkit



The WHO Human Health Risk Assessment Toolkit (WHO 2010) (https://www.who.int/ipcs/methods/harmonization/areas/ra_toolkit/en/) provides users with guidance for identifying, acquiring and using the information needed to assess chemical hazards, exposures and the corresponding health risks in their given health risk assessment contexts at local and/or national levels. The Toolkit contains roadmaps for conducting a human health risk assessment; identifies information that must be gathered to complete an assessment; and lists electronic links to international resources where the user can obtain information and methods essential for conducting the human health risk assessment.

The Toolkit has been developed for public health and environmental professionals, regulators, industrial managers and other decision-makers who have at least some training in the principles of risk assessment, and who have a role in assessing and managing the human health risks of chemicals.

Box 3.3 The OECD Environmental Risk Assessment Toolkit



The OECD’s internet-based Environmental Risk Assessment Toolkit (OECD 2016) (<http://www.oecd.org/env/ehs/risk-assessment/environmental-risk-assessment-toolkit.htm>) provides access to practical tools for the environmental risk assessment of chemicals. It describes the general work flow of environmental risk assessment and provides examples of risk assessments. Links are provided to relevant tools developed by the OECD and its member countries that can be used in each step of the work flow.

Assessment Toolkit (WHO 2010) (Box 3.2). The OECD has developed an Environmental Risk Assessment Toolkit (OECD 2016) (Box 3.3).

3.2 Conceptual and methodological risk assessment solutions are emerging

Weight of evidence and systematic review

In weight of evidence (WoE) evaluations a combination of information from several independent sources is used to provide sufficient evidence to meet an information requirement. The possibility to apply a weight of evidence evaluation, or a systematic review approach, in

chemical risk assessment is included in a number of regulatory frameworks, including in the EU (Ågerstrand and Beronius 2016). The weight given to the available evidence depends on factors such as data quality, consistency of results, nature and severity of effects, and relevance of the information. Since WoE evaluations require the use of scientific judgement, it is essential to provide adequate and reliable documentation (ECHA n.d. b).

Canada applies WoE and precaution in risk assessment. Both WoE and precaution are influenced by uncertainty, so that all three concepts – weight of evidence, precaution and systematic review – should be considered together in decision-making. As noted by the Government of Canada (2017b), “a limited

low quality data set will increase assessment uncertainty, reduce the strength and likely consistency of the WoE, thereby increasing the need to consider precaution. Conversely, a more robust data set will decrease uncertainty, resulting in the application of less precaution". A survey of frameworks for best practices in weight of evidence analyzes provides a review of 50 frameworks which have been used (Rhombert *et al.* 2013).

Systematic review (SR) is a formal technique for reviewing existing evidence in order to answer a specific research question. It uses a predefined, multi-step process to identify, select, critically assess and synthesize evidence from scientific studies to reach a conclusion. It does not replace scientific judgement; rather, it uses a process to document the basis for scientific judgements, minimizing the risk of bias and error and maximizing transparency (Roth and Wilks 2014). A Navigation Guide for the Systematic Review Methodology was published in 2014 (Woodruff and Sutton 2014)

The SR method is described in detail in a handbook published by the United States National

Toxicology Program (US NTP) (US NTP 2018a). The handbook will be updated as methodological practices are refined and evaluated and strategies are identified that improve the reliability, ease and efficiency of conducting systematic reviews. A recently published US EPA document on the application of systematic review in TSCA evaluations provides an overview of the general principles used (US EPA 2018d). Both weight of evidence and systematic review are useful to inform the risk management decision-making process and make it more evidence-based.

Defining better specific human and environmental protection goals

Protection goals in regulatory frameworks for chemical risk assessment and management are typically formulated in general terms. They demand, for example, avoidance of "harmful effects", "unreasonable risks" or "adverse impacts". However, hazard evaluations, exposure assessments and risk characterizations provide (often detailed) technical information that does not speak to broad protection goals. Therefore, it has been argued that specific protection goals should be better defined ("what to protect,



where and when”) to improve, in particular, the environmental risk assessment of chemicals (Brown *et al.* 2017; Maltby *et al.* 2017). Further work on Adverse Outcome Pathways and integrated approaches to testing and assessment would help advance the linking of traditional toxicity endpoints (which are studied for hazard assessments) to impacts considered in regulatory decision-making in regard to risk levels. Currently, specific protection goals are mainly used in frameworks for retrospective, site-specific risk assessments, as these allow the definition and evaluation of “acceptable” versus “unacceptable” effects on species, populations and ecological communities.

To move prospective risk assessment methods forward and better define environmental protection goals, the use of the ecosystem services concept has been proposed by the European Food Safety Authority (EFSA) in the risk assessment of plant protection products and other chemical products (EFSA 2010; EFSA 2016). This entails systematic evaluation of impacts on potentially vulnerable key populations of organisms (the “ecosystem service providing units”) and covers various dimensions. These may include biological entity, attribute, magnitude of effect, temporal and geographical scale of the effect, and the degree of certainty that a specified level of effect will not be exceeded. An ecosystem protection approach, if successfully implemented, provides a detailed map indicating conditions under which certain species groups might be at risk and what the overall impacts

on biodiversity might be. It therefore allows the definition of appropriate risk management options. However, this approach is extremely data-demanding and might be best suited to chemicals (e.g. plant protection products) for which rich data sets are available.

Improving risk assessment for chemical mixtures and cumulative exposures

Monitoring studies routinely show that humans, as well as organisms in the environment, are exposed to hundreds of individual chemicals from a variety of sources, resulting in cumulative exposures. Nevertheless, even modern regulatory frameworks mainly focus on the assessment of individual chemicals – disregarding the reality of cumulative exposures from different chemicals and products through different emission sources via a multitude of exposure pathways. Given that the risk of chemical mixtures in most cases exceeds the risks posed by individual chemicals, toxicological or ecotoxicological thresholds may not always be sufficiently protective (Kortenkamp, Backhaus and Faust 2009). There are GHS criteria for the classification of mixtures in which any impurities, additives or individual constituents of a substance which have been identified are considered if their properties exceed the cut-off value/concentration limit for a given hazard class (UN 2017).

The development and assessment of approaches and methods for mixture toxicity assessment have been subject to extensive reviews

Box 3.4 Assessing exposure to chemical mixtures: WHO and EFSA activities

The WHO has been developing frameworks for human risk assessment of chemical mixtures (OECD 2011; Meek *et al.* 2011; WHO 2017a; US ATSDR 2018). The key purpose of this work is to provide an overview of available tools and practical recommendations to support the screening and prioritization of mixtures for the assessment and management of risks to human health associated with exposure to chemical mixtures from drinking water and its sources.

The European Food Safety Authority (EFSA) has also carried out a number of activities in this field related to pesticides and contaminants. As a first step prior to an assessment, the EFSA considers the problem formulation, defining the relevant exposure, hazard and population to be considered. The risk assessment itself is, in practice, conducted using a tiered approach for exposure assessment, hazard assessment and risk characterization. The tiers can range from tier 0 (a data-poor situation, default values) to 3 (full probabilistic models). Higher tiers require increasing knowledge about the group of chemicals under assessment (Meek *et al.* 2011; EFSA n.d.).

and guidance (OECD 2011; Meek *et al.* 2011; WHO 2017a; United States Agency for Toxic Substances and Disease Registry [US ATSDR] 2018). In the future new methods such as high-throughput screening could play an increasing role. In order for these methods to fulfil their promise, they should have relevance for whole animal models. Empirical knowledge of typical exposure patterns and the underlying drivers of mixture toxicity is still scarce and fragmented. They are the subject of ongoing research and evaluation. Given the complexity of assessing combined exposures temporally and spatially, the data demands compared with traditional risk assessments increase exponentially. Yet simple, robust and sufficiently protective rules of thumb are needed in order to allow at least semi-quantitative risk estimates to be conducted in support of regulatory action. The concept of an additional safety factor is currently being addressed, for example, by KEMI in Sweden and the National Institute for Public Health and the Environment in the Netherlands (Backhaus 2015; van Broekhuizen, Posthuma and Traas 2016). In the WHO and the EFSA work has been carried out to develop a framework for assessment of combined exposures to multiple chemicals (Box 3.4).

Strengthening integrated risk assessments covering human health and the environment

Human well-being is closely related to ecosystem health and vice versa. It has become increasingly clear that media- or sector-specific efforts are insufficient to tackle broad-scale problems such as antimicrobial resistance development in the

environment. The WHO One Health initiative has been developed to address aspects of this issue (Box 3.5). In the United States, the National Toxicology Program is engaged in the SEAZIT (Systematic Evaluation of the Application of Zebrafish in Toxicology) initiative (US NTP 2018b). Small aquarium fish species such as the zebrafish are used as model organisms to replicate human development, physiology and disease processes while avoiding the limitations of use of rodent-based models. Generating data on aquatic models could help evaluate biological processes related to both ecological receptors and humans. Fully incorporating these aquatic model organisms into modern toxicological investigations could also yield significant scientific and economic benefits (US NTP 2017).

Better linking of risk assessment and risk management

The role of a risk assessor is to assess whether a risk of a certain chemical is “likely to arise”. The role of a risk manager is to assess the “acceptability” of that given risk and, if needed, recommend risk management options to ensure an acceptable risk situation, taking into account trade-offs between risks and benefits of the use of the chemical concerned. In general, it would be useful for risk assessment to be better guided by risk management options and objectives. For example, risk assessors could be asked to provide certain levels of certainty or uncertainty in their assessment with respect to various risk management options, which would be particularly beneficial under multiple-risk conditions that require the evaluation of integrative response

Box 3.5 The WHO One Health initiative

The WHO One Health initiative is an approach to designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes (WHO 2018a; World Organization for Animal Health [OIE] 2018). The WHO works closely with the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health to promote multi-sectoral responses to food safety hazards, risks from zoonoses, and other public health threats at the human-animal-ecosystem interface, and to provide guidance on how to reduce these risks. While One Health currently targets a selected number of issues, mainly at the interface of veterinary and human medicine, its approach could be extended to the development of truly integrated chemical risk assessments, as envisaged by the WHO when this initiative began (FAO 2011; WHO 2017b; OIE 2018).



options. This could be relevant, for example, when assessing the consequences of exposures to complex chemical mixtures or evaluating chemical alternatives. Detrimental risk-risk trade-offs, which might occur as a result of different amounts of hazard and exposure information being available for different chemicals, could be reduced (Sahlin and Rundlöf 2016). Already in 2009, the National Research Council in the United States published a report which recommended that risk assessments be more closely linked to problem formulation and problem solving, and that the level of detail in a risk assessment match the question that needed to be addressed (United States National Research Council [US NRC] 2009).

The WHO *Guidance Document on Evaluating and Expressing Uncertainty in Hazard Characterization* (2017c) finds that “the process of evaluating human health effects as a function of (potential) exposure [...] necessarily involves uncertainties” associated with extrapolating results from hazard assessment. “Ignoring these uncertainties may lead to incomplete risk assessments as well as suboptimal decision-making and risk communication.” Risk assessors therefore have to take uncertainty explicitly into account. “Effective risk assessment and subsequent risk

management does not require the elimination of uncertainty; rather, it requires that any such uncertainty is made visible and has been taken into consideration.”

Solution-oriented approaches in environmental risk assessment

Demand for solution-oriented approaches is increasing not only in the context of chemical risk assessment, but also in that of global environmental assessments generally (Jabbour and Flachsland 2017). To foster tighter coupling of chemical risk management with risk assessment in identifying appropriate action, the concept of solution-focused risk assessment has been proposed (Finkel 2011) (Box 3.6). van Wezel *et al.* (2017) used a solution-focused perspective for chemicals in European water bodies. Instead of another database on toxic effects and chemical exposures, they developed one that provides mitigation options for improving water quality. A solution-focused and systems-oriented approach, combined with such a mitigation database, offers a common, action-oriented perspective among stakeholders on the effects on water quality of possible mitigation options throughout a

Box 3.6 Solution-focused risk assessment (Finkel 2011)

Instead of beginning by asking “How bad is the problem?”, solution-focused risk assessment asks “How good are the solutions that could be applied to the problem?” Rethinking risk assessment this way could provide three types of benefits:

- › It could help to interrupt an endless cycle of analysis (sometimes referred to as “paralysis by analysis”). When the goal is to know enough to decide, rather than to “know everything”, natural stopping points may emerge.
- › It could lead sooner to decisions that succeed in reducing risk, rather than assessments of how much risk reduction would be optimal.
- › It could highlight ways to resolve multiple risks and, simultaneously, avoid unnecessary and poorly thought out risk-risk trade-offs.
- › Affected stakeholders might then be more easily involved in discussing what should be done to address the problem.

chemical’s life cycle in various sectors and at various locations in the water system.

Risk assessment, in its role of defining an “acceptable operating space” for industry and consumers (as a proactive tool to help avoid harm in the first place), might not be easily amenable to this approach, which seems best suited to media- and site-specific assessments in order to provide options for taking action as early as possible. When it has been demonstrated that a river is polluted by untreated effluents, or that decreasing fertility in a community is due to endocrine-disrupting chemicals, the application of this approach might be most useful, depending on national practices.

Risk communication

Communicating risk information is a challenge within countries and internationally. In order to be effective, risk communication needs to address psycho-social aspects of chemical risk perception and management. Since it is characterized by uncertainty, rapid changes and developments, risk communication requires flexible communication tools and channels. It should therefore, as appropriate, exploit new technology including social media. Two-way communication via interactive media also allows feedback that can help improve future risk communication policies and practices. Groups with whom effective risk communication is essential include workers, public authorities, health care providers and the media; the steps

to be taken before an accident occurs include providing information to the public about relevant chemical products (emphasizing the difference between hazard and risk) (OECD 2002).

In recent years technological advances have improved many types of scientific risk information dramatically. However, valuable information can easily go to waste if not effectively communicated to the people who need it so they can make decisions. Effective communication helps technical experts to develop and share data. It also enables professional users to understand the data, while it influences how many ordinary people take actions to reduce risk. Because communication is a process, it should be considered throughout every stage of risk assessment (United Nations Office for Disaster Risk Reduction [UNISDR] 2017). (See also Part III, Ch. 4 and, in relation to chemical accidents, Part III, Ch. 6)

3.3 How can risk assessment evolve?**Grouping of chemicals**

Currently, chemicals are most often assessed compound by compound. Risk assessments that evaluate whole chemical groups could substantially reduce the burden on the regulatory system and increase efficiencies in public and environmental health protection. Group risk assessments are currently limited to

complex chemical mixtures such as petroleum products. The OECD has developed guidance for the grouping of chemicals and read-across approaches (OECD 2014; OECD 2018). Although grouping is limited at this time to the hazard assessment of data-poor chemicals, it might be a starting point for the development of similar approaches for risk assessments. Canada has already used grouping strategies to assess nine key groupings of substances under the Chemicals Management Plan (Government of Canada 2016b). The European Commission and the ECHA are also looking at possibilities for the increased use of grouping of chemicals to speed up the identification and management of those of concern (KEMI 2018; ECHA n.d. c).

Research suggests the promise of the grouping methodology. The results of a recent study show that a combination of bioactivity and chemical descriptors can accurately predict a range of target organ toxicity outcomes in repeat-dose studies. Further experimental and methodological improvements may further increase predictivity (Liu *et al.* 2017). Another recent publication concludes that an *in silico* tool which can predict toxicity values with uncertainty of an order of magnitude or less can be used in combination with exposure assessment to assess risks of environmental chemicals quickly and quantitatively when traditional toxicity data or human health assessments are unavailable. This tool could fill a critical gap in the risk assessment and management of data-poor chemicals (Wignall *et al.* 2018).

One proposed generic risk-based approach is the concept of Threshold of Toxicological Concern (TTC). TTC assumes that an exposure below a certain threshold concentration (which is specific for a defined group of chemicals) is without adverse toxicological consequences (EFSA 2012). It has been used to define such exposure concentrations for the members of a given chemical class. This approach could also be particularly useful in deciding which chemicals should not be given high priority for further work. Full risk assessments would then only be required if the exposure level exceeded the TTC. An advantage is that applying the TTC would not require substance by substance hazard

data. However, its validity hinges on a valid chemical grouping, sound estimation of the TTC for each chemical group, and reliable exposure assessment. Canada has experience with using a TTC-based approach in a regulatory setting (Environment and Climate Change Canada 2016; Environment and Climate Change Canada and Health Canada 2017)

Better integration and harmonization

Chemical risk assessment is largely anchored in a national (regulatory) context, rather than being organized at the international level under an overarching framework as is the case with, for example, efforts to combat global climate change and protect the ozone layer. Efforts to address certain priority hazardous chemicals are implemented in a complex set of intertwined, legally independent treaties and programmes that address a small number of chemicals (Selin 2013). The lack of a holistic global strategy for chemical hazard and risk assessment and management also hampers knowledge transfer and transparency. Ways to fill this gap could be explored in the context of the sound management of chemicals and waste beyond 2020 (Backhaus, Scheringer and Wang 2018).

Improved integration and harmonization may also be valuable at the technical level (Wilks *et al.* 2015). Human health-oriented and environmental risk assessments use similar techniques, sometimes even employing identical (eco)toxicological test systems, chemical monitoring strategies and data integration/evaluation approaches. Better connecting human health and environmental perspectives in an integrated assessment by generating empirical data and models that consider both human health and environmental protection would vastly improve the efficacy of the risk assessment process.

The report *Using 21st Century Science to Improve Risk-Related Evaluations* (US NASEM 2017) makes recommendations for integrating new scientific approaches into risk-based evaluations. It proposes how best to integrate and use the emerging results in evaluating chemical risk and considers whether a new paradigm is needed for data validation; how to integrate the divergent

data streams; how uncertainty might need to be characterized; and how best to communicate new approaches so that they are understandable to various stakeholders.

Generic risk-based approaches

Conducting an in-depth chemical risk assessment can be resource-intensive. In certain cases, however, a generic and science-based, risk-based approach – which is less costly, but fit for purpose – can be used (Hansen 2017). For example, this approach could be used to identify:

- › chemicals with low exposure that are unlikely to present unreasonable risks;
- › low-hazard chemicals (e.g. chemicals that do not need to be classified according to the GHS criteria and therefore are unlikely to present unreasonable risks); and
- › combinations of hazards, uses and exposures that are likely to present risks.

Several strategies have been developed so that regulatory decisions can be taken (if circumstances permit) without requiring the full suite of hazard and exposure assessments. These approaches do not directly replace full risk assessments; however, they provide decision-making criteria for determining whether there is a case to answer and/or they often guide prioritization efforts. Canada, for example, has developed the Chemicals Management Plan Risk Assessment Toolbox, which offers a range of approaches to address substances (or groups) effectively by selecting an appropriate and fit-for-purpose approach. Such examples include the Rapid Screening Approach that may use either qualitative or quantitative data for assessments and are typically applied to substances that have lower potential for exposure and risk; or the adoption of existing hazard characterizations from international organizations (Government of Canada 2016b). A generic risk-based approach could also be to consider that there are combinations of hazards and uses for which risk is inevitable because exposure cannot be controlled, such as in the case of carcinogenic,

mutagenic and reprotoxic (CMR) chemicals in consumer products and preparations.

Methods which are only hazard-based are sometimes used in voluntary approaches, particularly when possibilities to substitute hazardous chemicals with less problematic alternatives are being explored. An example is use of the SIN (Substitute It Now!) List approach (International Chemical Secretariat n.d.). To a certain extent, eco-labelling is also based on the consideration of hazards. High-throughput screening for hazards, accompanied by read-across methods, can help to facilitate the prioritization of chemicals for a full traditional risk assessment.

Chemical assessment in countries with limited resources

In countries with limited resources, a number of economic, technical and administrative obstacles may impede the adaptation of elaborate risk assessment frameworks developed in countries with greater resources. The lack of an applicable, overarching international framework, and prevailing difficulties in the implementation of already existing instruments, pose additional problems. As it might not always be possible to make a full risk assessment, management on the basis of hazard is practised by some countries and is considered a legitimate approach to sound chemicals management in specific cases – including, for example, chemicals that are highly hazardous, that do not have thresholds, that are persistent or bioaccumulative, or that have non-monotonic dose responses, or where conditions of use are such that generic exposure assessments are not valid.

Towards enhanced knowledge-sharing

In the beyond 2020 chemicals and waste strategy, consideration could be given to how best to promote the best global use of the rapidly increasing volume of publicly available hazard and risk information. This could be achieved, for example, through continued technical harmonization of the scientific methods used in the generation and assessment of the necessary data, including harmonization of data



formats. The WHO Chemical Risk Assessment Network supports global efforts to assess and manage the risks associated with exposures to hazardous chemicals. Established in 2013, it involves institutions with chemical risk assessment activities (WHO 2018b). The use of existing OECD products in this respect could be considered. Countries with limited resources would then be better placed to benefit from the results, including priority-setting and in-depth assessments (generated and made publicly available through national and regional programmes), and to apply them in their national contexts.

3.4 Potential measures to further advance risk assessment

Taking into account the preceding analysis, stakeholders may wish to consider the following measures to further advance risk assessment:

- › Facilitate global use of the increasing volume of publicly available risk-related information, particularly by countries with limited resources.

- › Develop and adapt chemical risk assessment methods in order to facilitate their use in countries with limited risk assessment capacity.
- › Improve the knowledge base for environmental risk assessment (e.g. through chemicals release data).
- › Further develop risk assessment methods for chemical mixtures and chemicals in products, as well as integrated risk assessment approaches covering human health and the environment.
- › Explore further how screening-level, generic risk-based approaches can be used, where these approaches are fit for purpose.
- › Take steps to facilitate, where appropriate, the use of risk assessment methods in developing countries, in order to further develop and harmonize methods for the risk assessment of chemical mixtures and chemicals in products, and consider developing more specific protection goals for use in risk assessment.

4/ Risk management decision-making: making it work in all countries

Chapter Highlights

Safety data sheets and labelling, based on the GHS, provide the foundation for risk management. However, globally there are important implementation and knowledge gaps.

Regulatory decision-making can stimulate frontrunner companies to undertake sustainable innovations.

Government regulatory actions, non-regulatory strategies and voluntary initiatives may be mutually supportive when used in a concerted way.

Socio-economic analysis that addresses the costs and benefits of action and non-action is useful to inform decision-making. Nevertheless, caution in the interpretation of results is required.

The IOMC Toolbox for Decision-Making in Chemicals Management can assist countries in identifying the most appropriate risk management instruments and approaches.

Risk assessment is a scientific approach which provides decision-makers with robust assessments of the actual or potential impacts of exposure. It is an approach that takes socio-economic considerations into account. This chapter addresses important aspects of the chemical risk management decision-making process: information needs; the available support tools; how regulatory and voluntary actions can be complementary; and how countries with limited resources can engage in risk management (e.g. on the basis of the GHS).

4.1 From chemical risk assessment to risk management

Risk management decision-making is a process whereby risk managers, policymakers and scientists work together closely to find innovative ways to select the best option(s) for a course

of action to ensure that human health and the environment are protected. In most cases a chemical risk assessment is a solid basis for chemical risk management. The interface of the risk assessment and the risk management process is referred to as “risk characterization”. In risk characterization, exposure and hazard are compared in order to determine a No Observed Adverse Effect Level (NOAEL) – that is, the greatest concentration or amount of a substance found in a test to cause no adverse reactions by the target organism for a specific endpoint (further described in Duffus, Nordberg and Templeton 2007). Since the NOAEL is usually determined through animal testing, assessment factors are used to convert NOAELs to a reference dose that may be applied in human risk assessment and risk management.

The outcome of risk characterization is often presented in the form of a risk quotient that compares the (expected) concentration of a

chemical in the medium of interest (e.g. the human body, ambient air, an aquatic ecosystem) with the maximum concentration deemed safe under normal circumstances. Certain population groups are more vulnerable to exposure to chemicals due to biological, social, economic or other factors. These groups include, among others, the elderly, children, pregnant women and the poor. The possible risks for these vulnerable groups require special consideration in risk management decision-making, especially during the risk characterization process.

How much information is needed for risk management decision-making?

Risk assessment and risk management processes that aim at preventing harm to human health and the environment require a significant amount of scientific information. This information is, at times, characterized by uncertainty. In decision-making to protect human health and the environment, where there is incomplete knowledge or lack of scientific certainty, precautionary actions are often considered, in accordance with Principle 15 of the Rio Declaration on Environment and Development

Principle 15 states that “In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation” (UN 1992). A logical framework for using the precautionary principle in chemicals regulation has been developed to help regulators in the EU work through the process of considering whether a combination of concerns and uncertainties justifies taking precautionary measures of control (Milieu, T.M.C. Asser Institute and PACE 2011). This framework underlines the importance of documenting the evidence of concerns and uncertainties, so that the decision-maker can be confident that applying the precautionary principle is appropriate.

Addressing data uncertainties concerning the exact magnitude of the risk, as well as carefully considering options for the implementation of

risk management, can at times make the risk management process complex. While chemicals’ hazards cannot be changed, exposures can be controlled to eliminate or minimize harm to human health and the environment, a hierarchy can be used in applying controls. In the field of occupational health, for example, elimination/substitution of the hazard is a preferred approach and is at the top of the hierarchy. This is followed by subsequent steps, among which are engineering controls, administrative controls (including changes in work practices) and, finally, use of personal protective equipment (PPE) (US CDC 2015).

In controlling exposure, a number of information uncertainties also exist and must be taken into account. Reliable measurements of exposure are often scarce and limited to the workplace. While monitoring data could be used in exposure assessment, they are available for only 1 to 2 per cent of the chemicals on which there are some toxicity data (Egeghy *et al.* 2012). A further challenge in determining the risk of chemical exposure to human health or the environment is that information describing how chemicals are used does not always cover the whole life cycle. Fortunately, even when uncertainties exist and not all the desired information is available, the use of Emission Scenario Documents (ESDs) and models can in most cases help to provide the necessary insights (OECD 2018a; ECHA n.d. a). In the case of pesticides, surveillance programmes are also an important basis for risk management. Activities in these programmes include the investigation and evaluation of adverse health effects related to acute pesticide exposure and the analysis of pesticide exposure data.

4.2 Safety data sheets and labelling: implementation and gaps

Safety data sheets and labels: important tools for risk management

An important first step in risk management is to ensure good access by workers and consumers to chemical hazard and risk information. Such information is often made available in the form

of product labels, pictograms and safety data sheets (SDS) (Ta *et al.* 2010; Sathar, Dalvie and Rother 2016; ECHA n.d. b). SDS and labels are the basic hazard communication tools for hazardous chemicals as regards their manufacture, storage, transport and other handling interactions (Lee *et al.* 2012; Dalvie, Rother and London 2014). International Chemical Safety Cards (ICSC) are information tools prepared through a peer-reviewed process in order to provide safety and health information on chemicals in a clear and concise way (ILO 2018; WHO 2018a). By promoting safe use of chemicals in the workplace, these cards also support implementation of the ILO Chemicals Convention (ILO 2017).

Hazard and safety communication elements such as pictograms, hazard statements, precautionary statements and guidance, and a harmonized format for the preparation of SDS are the key constituents of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) described in Part II, Ch. 2.4 (UNECE 2017; UNECE n.d. a; UNECE n.d. b). The GHS is a common starting point that can help risk managers ensure the appropriate handling and safe use of chemicals (Dalvie, Rother and London 2014). Effective implementation of classification and labelling is an initial risk management measure that can, in principle, be implemented consistently in all countries even when limited resources are available. National or regional legislation on classification and labelling, based on the GHS, is necessary to ensure solid implementation and enforcement.

The GHS is (partly) in force in 72 countries. In some countries a transitional period is in effect before the GHS becomes mandatory. In other countries it has not yet been implemented (UNECE n.d. a) (see Part II, Ch. 3). Obstacles to fully harmonized implementation of the GHS include discrepancies in the classification process, and in the different information sources across countries and regions, mainly due to varying selections made from hazard testing and estimation results (Morita and Morikawa 2011) and legal implementation gaps (Persson *et al.* 2017). Continuous training on classification and awareness-raising in a global or regional setting would help governments to build expertise on



© UNITAR/Andrea Cararo, Labelling of containers in a leather chromium tanning factory

the implications of GHS, and to ensure that its provisions are reflected in legal instruments (Dalvie, Rother and London 2014).

While labels provide important first information to anyone who handles, uses, stores and/or transports hazardous chemicals, SDS provide more comprehensive information. They are product-related and enable the employer to develop and implement worker protection measures specific to the workplace (United States Occupational Safety and Health Administration [US OSHA] 2012; US OSHA 2013; UNECE 2017). There are, however, several gaps in the way SDS are prepared and applied in the workplace, meaning that workers may not be correctly informed and may be at risk. For example, studies show that many products contain chemicals that are not declared on the SDS, or that chemicals may be found at higher concentrations than indicated on the SDS (Nicol *et al.* 2008).

Where there is a mixture of chemicals, most SDS combine the hazards from all the components of the mixture, which may result in understating the actual risk in the event that synergistic effects result from the interaction between the components (ChemSafetyPro 2018; ECHA n.d. c). Similarly, an SDS may not address possible synergistic effects with other chemicals to

which workers may be exposed. Since chemical suppliers could be unaware of all possible applications of their chemical(s), precautions for use cited in the SDS may not be appropriate for all situations. It should also be noted that while SDS often reach the first producer of an article, in most cases they do not reach the next levels in the supply chain and are normally not provided to retailers and consumers, who will therefore be unaware of the information in the SDS (Massey 2008). A study by Safe Work Australia found that for nanomaterials only 18 per cent of SDS contained reliable information to appropriately inform an occupational risk assessment (Frangos *et al.* 2010).

Are hazard and risk communication tools well-understood?

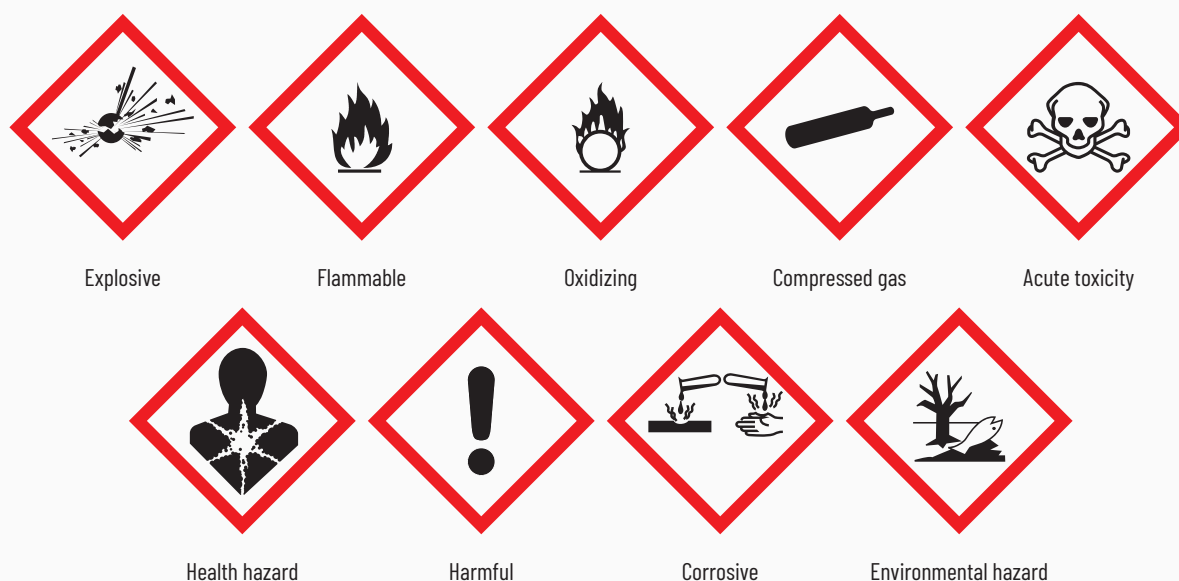
Chemical risk communication is of vital importance to make sure workers and the general population are well-informed and take protective measures in the use and handling of chemicals. In developing and evaluating the effectiveness of chemical risk communication tools, multidisciplinary expertise is required to ensure comprehensibility of chemical hazard information. Effective risk communication needs to take into account a range of aspects, including information sources, delivery channels, training

methods and the target audience. Figure 4.1 shows some frequently used pictograms.

Several studies have investigated the level of comprehensiveness of information on chemical hazards among workers and consumers. They have identified demographic characteristics, gender, level of education and cultural differences as some of the key factors that influence understanding of information on a label or an SDS (Sathar, Dalvie and Rother 2016) (see also Part III, Ch. 6). A study carried out in South Africa concerning the comprehensibility of chemical hazard communication elements revealed that understanding of hazard communication labels and safety data sheets was generally low. Symbols such as the skull and crossbones (98 per cent) and flames (93 per cent) were relatively well-understood (either correct or partly correct responses), but the majority of hazard symbols were of moderate to poor comprehensibility. There were significant levels of critical confusion (5 per cent or above) in the case of symbols for corrosive and compressed gases (Dalvie, Rother and London 2014).

Rother (2018) has identified a range of factors to ensure that information on pesticides' hazard and risk, as well as related safety measures, are effective, particularly in low- and middle-income

Figure 4.1 Hazard pictograms according to the GHS (UNECE n.d. b.)



countries. These factors include: a correct label must be on the pesticide container or packet; the label must be in the language of the end user; the end user must be literate and able to read the label language; the end user must be able to understand the content of the label (e.g. symptoms of poisoning); and the end user must have the means to implement the instructions (e.g. correct measuring and mixing instruments) as well as to apply safety precautions. Safety precautions include the use of correct PPE for the acute and chronic toxicity levels of the product, according to the relevant WHO and GHS hazard classification system (Rother 2014; Rother 2018). Consumers often assume that products with an eco-label or without hazard pictograms do not contain harmful substances (Hartmann and Klaschka 2017). These outcomes point to the need for well-considered information strategies to communicate chemical risks in consumer products.

Safety data sheets for nanomaterials remain a challenge

Engineered nanomaterials are a growing class of materials being manufactured and introduced into multiple business sectors (Eastlake *et al.* 2012). An evaluation of 97 nanomaterial-related SDS, according to the criteria set by the GHS, found that most of these SDS did not include sufficient information on the safety of nanomaterials such as their toxicity and physicochemical properties (Lee *et al.* 2012). It was concluded that this lack of information in the nanomaterial SDS could mainly be attributed to lack of toxicity and physicochemical property information on nanomaterials; unawareness of the effectiveness of conventional exposure controls, such as local exhaust ventilation and encapsulation or PPE, in protecting against nanomaterial exposure; lack of information on emergency and firefighting measures; and lack of knowledge on how existing



regulations apply to nanomaterials (Eastlake *et al.* 2012; Lee *et al.* 2012).

Guidelines published by the WHO offer several recommendations for protecting workers from the potential risks of manufactured nanomaterials (MNM). The guidelines address assessment of MNM health hazards and exposure, controls, health surveillance, and training of workers. One of the 11 recommendations is to assign hazard classes to MNMs on safety data sheets according to the GHS (WHO 2017).

4.3 Government action and proactive voluntary industry initiatives can complement each other

Government action and regulatory substitution goals can encourage voluntary initiatives

Governments are responsible, in the first place, for promulgating regulatory measures. They can also play an important role in fostering voluntary action in industry, for example by developing or promoting codes of practice, environmental quality objectives or guidelines, environmental release guidelines, or environmental performance agreements. The Canadian Chemicals Management Plan, for example, includes provisions for encouraging such non-regulatory initiatives (Government of Canada 2012).

Substitution goals set by public authorities can be a driver through facilitating voluntary frontrunner action. In Europe, the listing of substances of very high concern (SVHC) and the Candidate List for inclusion of substances for authorization under Annex XIV of REACH convey the intention of the regulator to take risk management action (ECHA 2011). In anticipation of such action, Hoffman-La Roche, for example, implemented a detailed global substitution action programme, which not only incorporates the necessary elements to comply with REACH in advance of regulatory timelines, but also uses business considerations and innovation practices to evaluate and test alternatives (Buxton 2016).

The OECD has developed a table of regulations and restrictions which includes substances/chemicals that are legally or voluntarily restricted or recommended for restriction by a number of stakeholders due to their hazards, or have been examined by jurisdictions based on potential concerns of a similar nature (OECD n.d.). It includes 55 lists of “chemicals of interest” from 12 categories of national or international legislation and programmes. These lists of substances/chemicals can be of general interest for voluntary substitution activities.

Advancing voluntary action beyond compliance can be an advantage

A growing number of industry-based voluntary initiatives that are led by individual enterprises or industry associations support, and in some cases go beyond, regulatory measures. These initiatives are based on, among others, the idea that voluntary action may in some cases be more flexible and cost-effective than regulations. Factors driving voluntary action of companies may include, for example: appealing to consumers who demand “green” products; pre-empting government regulations; seeking regulatory relief from regulatory action; or gaining a competitive advantage (Videras and Alberini 2007). Similarly, the importance of building confidence and trust in society and obtaining a “social licence to operate” encourages companies to take voluntary action and behave in a legitimate, transparent, accountable and socially acceptable way to lower risk for business (World Business Council for Sustainable Development [WBCSD] 2015).

Frontrunner companies can be found among the chemical industry, downstream sectors and retailers. Leading companies in the chemical industry, in downstream industries and in retail sectors have recognized the benefits and have initiated voluntary action, often ahead of potential regulatory action. These frontrunner companies can be considered as key drivers accelerating a transition to greener and sustainable chemicals alternatives in their sectors, at the same time addressing improvements in economic performance as well as the ecological footprint and potential health impacts of their products and production.

In the chemical industry a number of companies (e.g. BASF) have introduced portfolio sustainability assessments so as to act in a timely manner and make necessary changes prior to possible regulatory changes or new mandatory environmental or health requirements, in order to proactively steer their overall product portfolios towards improved sustainability outcomes (Consultancy.uk 2017). An example of proactive action in a downstream sector, the electronics industry, is the commitment by Apple to phase out brominated flame retardants and polyvinyl chloride in all its products, while other electronics companies have made partial progress by eliminating those substances in selected devices (Cook and Jardim 2017). S.C. Johnson, a formulator of chemical-intensive products widely used in households, launched a successful chemical classification process to rate raw materials based on their impact on human health and the environment (further explained in Part IV, Ch. 7).

In the retail sector major companies see “the value of getting ahead of the curve on enacting rules ahead of governments” and have therefore made significant progress in adopting safer chemicals policies. These policies drive reductions and substitutions of toxic chemicals in products and represent a commitment to publicly disclose all product ingredients in order to respect consumers’ right-to-know (GreenBiz

2018). Large retailers like Walmart in the United States, for example, stopped selling flooring products containing phthalates ahead of any future regulatory restrictions on these chemicals (Franklin 2015; Franklin 2016). Similarly, in Europe concerns about consumer safety and possible regulatory action triggered action by Coop Denmark to proactively replace certain fluorinated chemicals in food packaging products with a sustainable alternative (Green Science Policy Institute 2013). Many more examples of such actions have been described (Geiser 2015) (see also Part III, Ch. 4).

Ensuring the effectiveness of voluntary action

While voluntary initiatives can be useful, it is critical for governments to monitor the effectiveness of these initiatives, especially if they precede intended regulatory action. A certification and/or accreditation mechanism can help verify voluntary standards. Similarly, in certain cases conformity assessment of products by a public or private auditor could provide a check on the implementation of voluntary initiatives (Henson and Humphrey 2009). Depending on the outcomes of such monitoring, governments may need to reserve the position that regulatory follow-up can be put in place when envisaged policy objectives are not met or not met fast enough.



Responsible procurement as a vehicle for risk management and creation of markets for safer chemicals

It is well-recognized that responsible procurement and supply chain management (further discussed in Part IV) provide opportunities for public (and private) organizations to support practices that are likely to improve health and labour conditions, for example in those developing countries where production and processing often take place (Boström *et al.* 2011). An analysis of a global transition towards public spending on goods and services which maximizes environmental and social benefits indicates that commitment to implementation has increased (UNEP 2013). It describes the widespread use and recognition of public procurement as a key element driving innovation and sustainable development in all policy arenas. Similarly, demand for safer chemicals offers opportunities for private organizations to shift the marketplace towards more sustainable products and services.

A review based on case studies from several organizations, and their approaches to identifying and purchasing safer alternatives, describes the benefits and lessons learned from their sustainable purchasing programmes (Perlmutter 2015a). The Danish supermarket chain Coop, for example, works with suppliers to eliminate endocrine-disrupting chemicals and other chemicals of concern in products sold in its stores; Kaiser Permanente, active in the health

care sector in the United States, has developed a chemical score card and works with suppliers to eliminate or reduce the purchase of products that expose its workers and patients to toxic chemicals (Perlmutter 2015b). Organizations that offer products with safer chemistries need to know about potentially harmful substances in the intermediate products they purchase, and therefore have to engage on safety aspects with their suppliers and strengthen supply chain management in this respect. Eco-labelling can play an important role in this context, including by helping customers from both the public and private sector identify greener and more sustainable products, as further explored in Part IV, Ch. 7.

4.4 The potential of private standard-setting in international chemicals and waste management

International private standards and harmonization initiatives

The increasing complexity of global supply chains, and addressing risks across the supply chain, create challenges for traditional regulatory approaches and international policymaking. In a number of international policy arenas private sector standards have emerged as a complement, and a response to, deadlocks in global public action (Humphrey 2017). Prominent examples

Table 4.1 Forms of standards (adapted from Henson and Humphrey 2009) complemented with international examples relevant to chemicals and waste management

	Public	Private
Mandatory	Regulations Annexes A and B of the Stockholm Convention on Persistent Organic Pollutants (POPs) OECD Council Decision on Mutual Acceptance of Data (MAD)	Legally (or policy) mandated private standards International standards for flammable low global warming potential (GWP) refrigerants recognized by Parties to the Montreal Protocol
Voluntary	Public voluntary standards Globally Harmonized System for the Classification and Labelling of Chemicals (GHS) Codex Alimentarius Commission	Private voluntary standards Responsible Care® Manufacturing Restricted Substance List (MRSL) of the Zero Discharge of Hazardous Chemicals (ZDHC) Programme

include the Forest Stewardship Council, the Marine Stewardship Council (Humphrey 2017), and private governance in international forest regulations (Bernstein and Cashore 2007).

Public and private standards can operate and interact in different ways. Four forms of public and private standards can be identified, as shown in Table 4.1 (Henson and Humphrey 2009). While public standards are developed through a formalized process, and adopted by public bodies, private standards can be more broadly conceived as “written documents adopted by a non-governmental entity which lays down rules, guidelines and/or characteristics, for common or repeated use, for products or related processes and production methods, including transport” (Scott *et al.* 2017).

Private standard-setting relevant to chemicals and waste management

Several types of private standards can be distinguished: individual company standards, collective national standards, and collective international standards (Henson and Humphrey 2009). Concerning international private standards, a number of initiatives in recent years have sought to advance harmonization for specific aspects of the sound management chemicals and waste that are not addressed through treaty law or international (public) bodies. Initiatives are driven by the chemical industry or specific downstream industry sectors, or include initiatives cutting across industry sectors. They have been advanced through a range of fora, raising the question of how linkages with relevant private standard-setting may be established under a future approach on chemicals and waste management beyond 2020.

An example of private governance and standard-setting in the chemical industry dating back to 1985 (and currently covering 68 countries) is Responsible Care®, which is supported by the International Council of Chemical Associations (ICCA) (ICCA 2015). Responsible Care® is a voluntary commitment by the global chemical industry to drive continuous improvement and achieve excellence in environmental, health and safety and security performance. In 1995 the

chemical distribution industry officially joined the programme (International Chemical Trade Association n.d.). The Responsible Care Charter has been signed by CEOs representing more than 96 per cent of the world’s largest companies. In the United States, a Responsible Care® Management System has been established that includes independent third-party certification and transparent reporting and performance metrics (ICCA 2015). This approach has the potential to serve as the benchmark for monitoring and assessing implementation in other countries.



A more recent example of an international harmonization initiative in the chemical industry is the cooperation of leading chemical companies in the World Business Council for Sustainable Development to publish a common approach for conducting Portfolio Sustainability Assessments (PSA). Companies engaged in developing the standard expect that harmonizing PSA approaches will increase the robustness and credibility of company efforts, building on leading best practices. Harmonization is also expected to reduce complexity for external stakeholders and enable consistency in communicating results, including the use of shared language

on sustainability-related benefits and concerns throughout value chains and industries (WBCSD 2018). An example of private standard-setting in a downstream sector (the textile, leather and footwear industry sector) is the ZDHC initiative (see Part IV, Ch. 7).

A private sector harmonization initiative that cuts across industry sectors is the Proactive Alliance, which seeks to develop a common approach for collecting and sharing material data for articles (including their chemical composition) across sectors (Stringer 2018). This initiative addresses the fact that many sectors have their own material declaration systems, but currently do not communicate or share information between companies in different sectors despite many suppliers selling the same articles and components to multiple sectors. The automotive, chemicals, furniture, childcare products, electronics, mechanical, metalworking and metal articles, home textiles, textiles, sporting goods and medical devices sectors are among those engaged in the initiative.

Opportunities to recognize and strengthen private standards under a beyond 2020 approach

Since stakeholders are negotiating an approach for chemicals and management beyond 2020, there may be value in exploring the extent to which private sector standard-setting could be encouraged, as well as how relevant initiatives by the chemical industry, or downstream industry sectors, could be recognized under a global approach, including monitoring of the progress made. If, as may be anticipated, a future global beyond 2020 approach continues to have a multi-sectoral and multi-stakeholder orientation, dialogue and consultation with civil society organizations have the potential to improve the robustness of the initiative and increase legitimacy. Of equal interest may be the question of how to scale up participation by stakeholders and industry in all regions of the world, with the goal that common and harmonized approaches will ultimately enjoy universal participation.

4.5 Regulatory decision-making drives innovation

Lessons from international initiatives

The Montreal Protocol on Substances that Deplete the Ozone Layer, which came into force in 1989, is generally considered a very successful example of international environmental leadership (Canan *et al.* 2015). The prospect of international regulation of ozone-depleting substances offered DuPont, the world's dominant producer of chlorofluorocarbons (CFCs) up to the 1980s, the possibility of new and more profitable markets at a time when the production of CFCs was losing its profitability and promising alternatives had already been identified (Maxwell and Briscoe 1997). The company invested more than US dollars 500 million in developing and commercializing CFC alternatives and rapidly implemented new technologies (Rotman 2007; DuPont 2015).

Response to the Montreal Protocol illustrates the potential benefits of global policies that address the sound management of chemicals and waste by stimulating innovation, investment in research and development, awareness-raising and technology transfer. Since it entered into force, countries have continuously made efforts to take further steps and to address more ozone-depleting substances. International activities are being carried out to meet remaining challenges in reducing emissions of ozone-depleting substances while, at the same time, reducing emissions of greenhouse gases (GHGs). Replacing hydrofluorocarbons (HFCs), which are not ozone-depleting chemicals but have high global warming potential (GWP) values, will have additional benefits with respect to combating climate change (United States National Aeronautics and Space Administration 2015; UNEP 2016; US EPA 2016).

Innovative approaches adopted by governments and industry within the framework of the Montreal Protocol have resulted not only in a high rate of replacement of ozone-depleting GHGs by more environmentally friendly alternatives, but also in increased product efficiency (Eklund *et al.* 2013). Moreover, the regional networks of

National Ozone Units (government units in developing countries that are responsible for managing national programmes to comply with the Montreal Protocol) continue to strengthen regulatory action through fruitful collaboration among stakeholders (UNEP 2018).

Lessons learned from national initiatives

Decision-making which foreshadows a transition towards the substitution of hazardous chemicals by safer chemical and non-chemical alternatives is a driving force for academia and industry to initiate research to develop such alternatives. In the EU and the United States (in states such as Washington, Maine and California) chemical management regulations require assessments of chemicals that are classified as being of priority or of very high concern in order to evaluate the potential for safe and feasible substitutions (Jacobs *et al.* 2015).

One study (EC 2015) has suggested that REACH registration requirements were a main driver behind an increasing focus on safer and more environmentally friendly chemicals in research and innovation. Other forms of innovation identified by private enterprises have included increased knowledge of chemical safety; awareness of needs upstream and downstream in value chains; and improved risk management procedures. Another study (Berrone *et al.* 2013) found that institutional pressures can trigger innovation, especially in companies which are relatively more polluting. These studies suggest that governments can stimulate innovation, leading to environmental improvements, by discussing their regulatory intentions at an early stage with stakeholders.

The Center for International Environmental Law examined the impacts in the EU and the United States of laws concerning hazardous chemicals in terms of innovation. It found that the prospect of stricter laws significantly sparked the invention, development and adoption of alternatives. For example, exponential growth in the number of patented inventions for alternatives to phthalates was identified from 1999 onwards, coinciding with the adoption of stricter measures concerning their use (Center for International Environmental

Law 2013). On the other hand, very prescriptive, rigid regulation can hamper innovative activity by reducing the attractiveness of engaging in R&D, constraining modes of commercialization, and creating lock-in effects that require adherence to suboptimal standards (Pelkmans and Renda 2014).

4.6 What are the opportunities for moving forward on risk management decision-making?

Recent developments concerning the burden of proof of chemical safety

In a significant number of countries chemicals management legislation has been established that requires industry to provide a certain amount of safety information about a chemical that has been (or is planned to be) placed on the market. Based on a judgement about whether there is unacceptable or unreasonable risk, authorities then determine whether the chemical is safe for the intended use, or whether more information or regulatory action is needed. Information gaps and uncertainties can, however, make it difficult for authorities to perform a complete science-based risk assessment (Lofstedt 2011).

A number of regulations have been updated. A recent comparative study of regulatory reforms in the EU and the United States (Botos, Graham and Illés 2018) describes the main drivers leading to updates in the regulation of industrial chemicals. In the EU, changes in the regulation of hazardous substances under REACH have focused on remedying the problems of lack of data on the safety of chemicals; the need to speed up prioritization and risk assessment/management tasks; and the need to implement the polluter pays principle. As early as 1997, discussions began on whether the burden of proof of safety could be reversed (Hansson 1997). This has occurred, for example, in the EU under REACH, which places the burden of proof on companies, requiring them to identify and manage the risks linked to the substances they manufacture and market in the EU. They must demonstrate how the substance can be

safely used and communicate risk management measures to users (ECHA n.d. d). This type of approach reduces the resource burden for authorities by placing responsibility on companies. In particular, countries with limited resources may consider the option of developing or updating chemicals legislation, taking into account burden of proof considerations.

Risk management decision-making based on generic considerations, hazard properties and impacts

Regulators often prefer to use risk assessments as the basis for developing, analyzing and comparing regulatory options, and for selecting and implementing the optimal decisions; thus, they can identify the instrument or mix of instruments that is best suited to help achieve the risk management objectives on a sustained basis (Government of Canada 2016; ECHA n.d. e). However, management decisions can also be based on the hazard and generic risk considerations discussed earlier, which may be simpler given that hazard information is an intrinsic chemical property about which information is globally accessible.

The classification of chemicals in GHS categories is based on hazardous properties. It is an example of hazard-based management. If a substance itself, or one in a mixture, has a specific hazard, the hazard should be communicated to users in order to alert them to the possible risks arising from its use. This helps to manage risks: for example, gloves might be worn in the case of substances that are skin irritants. It can also be argued that management action could be taken based on endocrine disruption or carcinogenic, mutagenic or reprotoxic (CMR) properties. A cancer hazard identified by the International Agency for Research on Cancer (IARC) gives regulators strong indications of necessary management action (IARC 2018).

A close look at chemicals legislation in which both hazard- and risk-based practices are considered (e.g. REACH) suggests that these approaches do not necessarily conflict. Instead, they can be seen as complementary means of informed decision-making (Hansen 2017). For example, guidelines for toxicity testing and the criteria for classification set an upper dose limit above which exposure can no longer be assumed to be reasonable and no testing is done; animal welfare is also a factor in this regard. This is described in the guidelines as the application of the “limit test”. In addition, this information is used when deciding on whether to classify a substance. Within the EU chemicals management framework (for industrial chemicals, plant protection products, biocides, and classification, labelling and packaging [CLP]) “hazard-based” and “risk-based” approaches can be seen as based on the same principles.

Alternatively, there are also approaches for exposure-based priority-setting (Egeghy *et al.* 2011). In this context very persistent and very bioaccumulative properties can be drivers to consider action. In light of the often limited resources available for risk management, it might be useful to consider the extent to which less resource-intensive approaches (e.g. hazard-based ones) could accelerate decision-making regarding the sound management of chemicals. In this respect, it might be helpful to bring together the combined expertise of the Inter-Organization Programme for the Sound Management of



Chemicals (IOMC) (WHO 2018b) participating organizations and develop globally applicable guidance.

Risk management based on hazard assessment is advancing in the retail sector. Consumers increasingly demand safe and healthy products, as well as transparent information (e.g. about “food miles”). This has led many large retailers to consider offering “toxic-free” consumer products as being good for business. To that end, leading companies are initiating (and requiring from their suppliers) the use of hazard assessment approaches as a means to differentiate products and ingredients with lower versus higher hazards, or to certify “greener” chemical ingredients in their consumer products (Box 4.1). Hazard is therefore used as a basis to address consumer concerns about chemical safety and to manage the safety of products offered for sale by the retailers concerned.

Using socio-economic assessment in decision-making

Socio-economic assessment (SEA) is used in a number of risk management decision-making processes. Many legislative frameworks for chemicals management request that it be used as an established method of weighing the pros and cons of an action for society as a whole when decisions are taken on management options. An SEA should be carried out in a transparent way, using distinct analytical parameters. It can add particular value when the benefits of regulation or

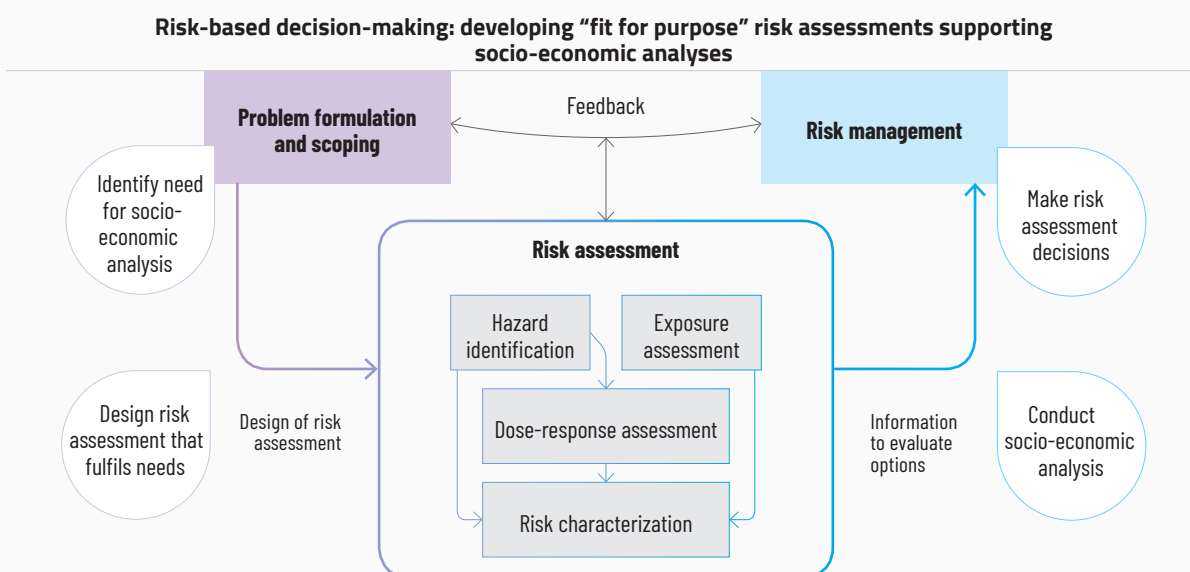
pollution prevention can be calculated, and when the risk assessment includes specific exposure data as well as explicit conclusions from hazard identification and dose-response assessments (Chiu 2017) (Figure 4.2). The outcomes of an SEA can also be helpful in the communication and justification of actions, and in facilitating transparency in the decision-making process (OECD 2016). The ECHA and the US EPA have developed guidance for use in SEA (ECHA 2017; US EPA 2018).

In recent years significant methodological progress has been made in assessing the costs and benefits of managing the risks of chemicals. Further work is required, particularly concerning the need to obtain better information to evaluate the benefits for human health and the environment of possible regulatory action. For example, when information is available, opportunities to better support SEA include providing population variability estimates in exposure assessment; using more formal approaches in evaluating the evidence for causal relations between exposure and specific effects; and applying probabilistic methodologies to make predictions of dose-response (Chiu 2017).

For environmental policy decision-making, cost-benefit analysis can be used to consider the case for the (social) efficiency of decisions within the broader policy process. This would involve understanding what the decision options provide in terms of benefits (defined as increases of human well-being) and costs

Box 4.1 Tools used by retailers to identify hazardous chemicals in their products and to select safer and greener alternatives

Many tools exist to assist companies in finding safer and greener chemicals to use in their supply chains. One example is the much-used GreenScreen®, a globally recognized tool that identifies hazardous chemicals and safer alternatives (GreenScreen 2018). The Chemical Footprint Project (CFP) is an initiative of investors, retailers, government agencies, non-governmental organizations (NGOs) and health care organizations that aspire to support healthy lives, clean water and air, and sustainable consumption and production through the effective management of chemicals in products and supply chains (Rossi *et al.* 2017). The Green Chemistry and Commerce Council (GC3) is a multi-stakeholder collaborative that drives the commercial adoption of green chemistry through catalysing and guiding actions across all industries, sectors and supply chains (GC3 n.d.). Various organizations, including retailers and business groups, often use a suite of tools to evaluate chemicals in products. These have been listed and reviewed by Gauthier *et al.* (2014) and Panko *et al.* (2017).

Figure 4.2 Risk assessment and socio-economic assessment (SEA) (adapted from Chiu 2017, p. 11)

(defined as reductions of human well-being) (Atkinson *et al.* 2018). Such cost-benefit analysis could be improved when countries have clear legislative requirements for its use and its role in the decision-making context, and when clear decision-making rules are in place that are transparently communicated. Proposals for marketing restriction usually need to contain a description of the risks, as well as information on health and environmental benefits, associated costs, and other socio-economic impacts. Such analysis is also important for policymakers in justifying the value of investing public funds in a chemical management system. There is an ongoing OECD project on the Socio-economic Analysis of Chemicals by Allowing a better quantification and monetization of Morbidity and Environmental impacts (SACAME). Several case studies and analyses have been developed to help countries advance in this field (OECD 2018b). Cooperative action by countries would allow mutual learning about the practical application of SEA methodologies and enable their further development from an applied perspective (OECD 2016).

SEA can also be important in decision-making on the risk management of chemicals in developing countries. A holistic and quantitative SEA case study, using a developing country-specific SEA framework and similar methodology,

was applied in China in the phase-out of hexabromocyclododecane (HBCD), a brominated flame retardant, under the Stockholm Convention on Persistent Organic Pollutants (POPs) (Zhu *et al.* 2016).

Use of market-based instruments in chemical risk management

An analysis of pesticide tax schemes in several European countries examined the importance of applying market-based instruments to reduce risks in agricultural systems (Böcker and Finger 2016). For the countries being compared it was found that even if the effectiveness of pesticide taxes appeared to be limited, a high enough tax on a specific pesticide would significantly reduce its application and the associated risks. In Sweden, for example, a simple, fixed tax scheme has been used since the 1980s. A tax on the use of pesticides was introduced in Denmark in 1965; since 2013 this tax has been based on environmental load (Pedersen 2016). A number of other European countries have also implemented pesticide levies or taxes. When there are adequate economic, political and environmental conditions, a highly differentiated tax scheme is potentially an effective instrument in the long term to reduce the load of hazardous pesticides and contribute to Integrated Pest

Management (IPM) (see also Part IV, Ch. 5 for fiscal incentives and market-based instruments).

Market-based instruments can be used in combination with command and control regulatory measures (e.g. prohibitions or restrictions) by accelerating the phase-in of alternatives during a transition phase until a substance is prohibited. While the use of market-based instruments in advancing the management of hazardous chemicals and waste is still limited, it has the potential to increase. Financial institutions can also help advance chemical safety. With respect to financing, the International Finance Corporation has a Sustainability Framework which includes performance standards applied to all investments and clients whose projects undergo a credit review process (International Finance Corporation 2012). In another context, a particular challenge emerges in reforming subsidy programmes that are creating incentives to use chemicals (e.g. increasing use of fertilizers to boost agricultural production) (Tan 2005; Bartelings *et al.* 2016).

What are the challenges and opportunities for countries with limited resources?

Effective implementation of risk management instruments and measures differs among countries, depending to a large extent on the amount of resources that can be made available to put the necessary structures in place (OECD 2015). Countries with limited capacities and resources face important challenges in setting up chemicals management programmes (Wang *et al.* 2016). For example, a study carried out in Tanzania (Stockholm Environment Institute [SEI] 2014) found that significant problems related to misuse of chemicals in the agricultural sector, wood preservation and small-scale mining persisted. It reported that an institutional issue to be tackled was improving national coordination.

In addition to the success story of the Montreal Protocol, the Basel, Rotterdam and Stockholm Conventions have provided important support to national governments and other stakeholders through scientific and technical guidance to address certain industrial chemicals, pesticides and their associated wastes. Not only has the

implementation of these Conventions led to a number of concrete global risk management actions. They have also been instrumental in strengthening national capacities for risk management. Implementation of the Minamata Convention is expected to provide additional benefits (see Part I, Ch. 8).

Countries with limited resources for risk management may consider starting with the implementation of the GHS and then making this part of an overall national chemicals strategy, rather than a stand-alone project. The development of the legislation needed for GHS implementation involves many sectors. Therefore, the multi-stakeholder platform created could serve as a basis for further discussions on chemical risk management. Concretely linking GHS implementation to the 2030 Agenda for Sustainable Development could also increase political support for chemical management at the national level (SEI 2017).

UNEP's Guidance on the Development of Legal and Institutional Infrastructures and Measures for Recovering Costs of National Administration for Sound Management of Chemicals (known as the LIRA Guidance) aims to provide practical support to policymakers to strengthen national legislation and institutional arrangements for achieving sound management of chemicals. The main objective of LIRA is to support countries in the process of developing national plans for strengthening legal and institutional infrastructures to govern the placing of chemicals on the market as part of a life cycle chemicals management policy. It includes proposals for measures to finance necessary administrative activities in this regard (UNEP 2015).

The IOMC Toolbox for Decision-making in Chemicals Management, which is internet-based, enables countries to identify the most appropriate and efficient actions to solve specific national problems related to chemicals management (Box 4.2). The Toolbox guides users towards cost-effective solutions which can be adapted to a particular country. It presents relevant IOMC resources, guidance documents and training material, all of which are available online and free of charge. In the Toolbox there are currently

Box 4.2 Decision-making for industrial chemicals: the IOMC Toolbox

The IOMC Toolbox (<https://iomctoolbox.oecd.org/>) identifies appropriate actions and guidance for the following:

- › a national management scheme for pesticides;
- › an occupational health and safety system;
- › a chemical accident prevention, preparedness, and response system for major hazards;
- › an industrial chemicals management system;
- › a classification and labelling system;
- › a system to support health authorities in the public health management of chemicals; and
- › Pollutant Release and Transfer Registers.

The Toolbox also provides links to the following five new online toolkits:

- › the OECD Environmental Risk Assessment Toolkit;
- › the WHO Human Health Risk Assessment Toolkit;
- › the FAO Toolkit for Pesticides Registration Decision Making;
- › the UNIDO Toolkit on Chemical Leasing; and
- › the UNIDO Toolkit on Innovative, Safe and Resource Efficient Application of Chemicals in Industry.

seven management objectives that can be selected (OECD 2018c). For each management objective, options requiring limited, medium and high levels of resources are included. The Toolbox also provides interactive features allowing governments to use it as a platform for collaboration among ministries, agencies, and other stakeholders such as industry.

4.7 Potential measures to further advance risk management decision-making

Countries could cooperate further to facilitate the use of more efficient chemical risk management approaches in countries that have limited resources, including through full implementation of the GHS, which would provide a basis for risk management decision-making in all countries. Taking into account the preceding analysis, stakeholders may wish to consider the following measures to further advance risk management decision-making:

- › Improve access to (and understanding of) chemical hazard, exposure and risk information by relevant stakeholders, including workers and consumers.
- › Increase international cooperation in order to facilitate worldwide implementation of the GHS, and explore the importance of GHS implementation for relevant SDG targets.
- › Refine and scale up the use of socio-economic analysis in risk management decision-making, including for application in developing countries.
- › Promote voluntary risk management initiatives to complement regulatory measures.
- › Evaluate the need to strengthen risk management approaches in line with national priorities.
- › Further develop innovative regulatory approaches to drive innovation to design safer chemicals.

5/ Assessment of chemical and non-chemical alternatives: focusing on solutions

Chapter Highlights

Regulatory actions, public pressure and voluntary initiatives drive the identification, evaluation and adoption of safer alternatives to chemicals of concern, in both products and processes.

Conventional approaches focus on reducing exposure to an acceptable level and evaluating drop-in replacements. Replacements often are of the same chemical class and have the same hazards.

Informed substitution aims to provide a safer functional match, including non-chemical alternatives, either through chemical replacement or through a process or technological change.

Alternatives assessments aim to focus on solutions and provide information to avoid regrettable substitutions, as well as to transition to more sustainable chemicals, materials, products and practices, often incorporating holistic sustainability assessment and life cycle thinking.

Challenges to robust assessment of alternatives, and the adoption of substitutes, include a lack of supportive policies, insufficiently mature methodologies, data gaps and limited experience

Chemical alternatives assessment has emerged as an important dimension of chemical risk management. It is a forward-looking and problem-solving means of identifying, evaluating and adopting safer alternatives to hazardous chemicals in products and processes. Safer alternatives can include safer chemicals and non-chemical alternatives, as well as changes in process, design and systems that lead to the informed substitution of chemicals of concern. This chapter introduces the latest developments in chemical alternatives assessment approaches; discusses how informed substitution of hazardous chemicals by safer alternatives can be an efficient and effective means of managing chemical risks; and identifies opportunities for future action.

5.1 What are the drivers for evaluating and adopting safer alternatives?

Momentum is increasing to remove chemicals of concern from processes and products

Both regulatory and non-regulatory drivers are providing momentum for the removal of chemicals of concern from manufacturing processes and from products. Non-regulatory drivers, such as consumer concerns, and pressures from NGOs (e.g. Greenpeace's global campaign focusing on toxic chemicals in the textile industry) have stimulated market demand for the removal of toxic chemicals in a wide variety of consumer product sectors (Grappi, Romani and Barbarossa 2017; Hartmann and Klaschka 2017; Greenpeace International 2018). A number

of large retailers, including Walmart, Target and The Home Depot in the United States, have announced strategies to reduce the presence of chemicals of concern in the products they sell (Brown-West 2017; MacCarthy 2017; Sturcken 2017; United States Natural Resources Defense Council 2018; Walmart 2018). How government action and regulatory substitution goals can encourage voluntary initiatives is addressed in Part III, Ch. 4.

A number of regulatory programmes, including in the EU and the State of California in the United States, require that manufacturers conduct alternatives assessments for chemicals of high concern (EC 2006; State of California Department of Toxic Substances Control [California DTSC] 2009; California DTSC 2017). At the international level, treaties such as the Montreal Protocol on Substances that Deplete the Ozone Layer and the Stockholm Convention on Persistent Organic Pollutants have specific provisions for the analysis of alternatives that could be substituted. These treaties provide critical stimuli for substitution by countries and global corporations (see also section 5.4 below).

5.2 Informed substitution: a critical chemical risk management approach

From conventional risk management to informed and functional substitution

In conventional chemical risk management strategies, it is typically assumed that use of a toxic chemical is a given. Consequently, these strategies often focus on controlling exposure to an acceptable level, as informed by risk assessments. Many chemical substitutions to date have focused primarily on individual chemicals, chemical classes or product types rather than on the functional uses of chemicals (e.g. as solvents, preservatives, surfactants or flame retardants). Although policies focused on substitution may consider chemical function, or functional use, in order to frame the technical evaluation of alternatives, the concept of functional use has not traditionally been used as a basis for policy (US NRC 2014).

The goal of informed substitution is to replace a chemical with a functional match (one which is



© USAID/John Healey, Ruth Mushingé prepares her mosquito net in her home near Mundabi, Zambia

Table 5.1 A functional substitution approach for chemicals in products and processes (Tickner *et al.* 2015, p. 744)

Functional substitution level	Chemical in product Bisphenol A in thermal paper	Chemical in process Methylene chloride in degreasing metal parts
Chemical function (Chemical change)	Is there a functionally equivalent chemical substitute (i.e. chemical developer)? Result: Drop-in chemical replacement	Is there a functionally equivalent chemical substitute (i.e. chlorinated solvent degreaser)? Result: Drop-in chemical replacement
End Use function (Material, product, process change)	Is there another means to achieve the function of the chemical in the product (i.e. creation of printed image)? Result: Redesign of thermal paper, material changes	Is there another means to achieve the function of the process (i.e. degreasing)? Result: Redesign of the process (e.g. ultrasonic, aqueous)
Function as service (System change)	Are cash register receipts necessary? Are there alternatives that could achieve the same purpose (i.e. providing a record of sale to a consumer)? Result: Alternative printing systems (e.g. electronic receipts)	Is degreasing metal parts necessary? Are there alternatives that could achieve the same purpose (i.e. providing metal parts free of contaminants for other end uses)? Result: Alternative metal cutting methods

safer for humans and the environment) through chemical replacement, or through a process or technological change that can eliminate the use of that chemical. Informed substitution employs a systematic process that uses the best available information to make choices about substitutes (Lavoie *et al.* 2010; US NRC 2014). It assumes that the function of a toxic chemical can be carried out using a safer option, which could be a different chemical or a completely different technology. In a given application it is the function provided by a chemical that is needed, not necessarily the chemical itself. Considering chemical function, rather than simply comparing the risks of drop-in chemical alternatives, offers a means of identifying a broad range of options to meet a particular functional need: this is referred to as “functional substitution” (Table 5.1).

When safer options are not available, research can be undertaken to investigate the use of safer chemistries (e.g. green or sustainable chemistry; see Part IV, Ch. 1) or to develop engineering or design solutions. This is consistent with the precautionary principle, the source reduction approach inherent in cleaner production and in the industrial hygiene hierarchy of controls – concepts that evolved in the 1990s (O’Brien 2000; Ashford 2013).

A functional substitution approach also makes it possible to open up to broader societal considerations, including whether a given

function is needed or whether the technical requirements for a function are too stringent. An example is the current debate about flame retardancy standards, and whether those standards that require the addition of chemical flame retardants are necessary to meet fire protection goals (Babrauskas *et al.* 2012; Israel 2013; State of California Department of Consumer Affairs 2014; Baker 2018). Special considerations might apply to pesticides. Social and cultural characteristics and long-term economic and environmental sustainability are important aspects of alternatives assessment in this case. Here it is not just a question of replacing one chemical with another, as it might be in an industrial process. The consideration of agroecology-based alternatives for highly hazardous pesticides was emphasized at the fourth session of the International Conference on Chemicals Management (Secretariat of the Strategic Approach to International Chemicals Management 2015).

Alternatives assessment

Alternatives assessment has emerged as a preferred process to support informed substitution. It is an iterative, step-defined and solutions-oriented process for identifying and comparing potential chemical and non-chemical alternatives that could replace chemicals of concern on the basis of their hazards, performance and economic viability

Table 5.2 Components of an alternatives assessment (US NRC 2014; Geiser *et al.* 2015)

Component	What it involves
Scoping, problem formulation, identifying alternatives for consideration	Establishes the scope of (and plan for) the assessment; identifies stakeholders to be engaged and decision rules that will guide the assessment; gathers data on the chemical of concern, its function and application; determines assessment methods and identifies alternatives to be considered.
Hazard/comparative exposure assessment	Evaluates human health and environmental hazards and assesses comparative exposures.
Hazard/comparative exposure assessment	Assesses the performance of alternatives against the requirements established during the problem formulation step above.
Economic feasibility assessment	Assesses the economic feasibility of alternatives against the requirements established during the problem formulation step above.
Other life cycle considerations	Addresses additional factors critical for determining risks to human health and the environment beyond those included in the hazard/exposure assessment component to avoid risk trade-offs (e.g. energy, climate change impacts).
Decision-making	Identifies acceptable alternatives based on information compiled in previous steps. Addresses situations where no alternatives are currently viable by initiating R&D to develop new alternatives, or improve existing ones, and establishes an implementation and adoption plan to identify potential trade-offs during adoption.

(US NRC 2014; Geiser *et al.* 2015) (Table 5.2). Alternatives assessment is used to provide critical information, in a systematic and continuous-improvement manner, that informs the choice of alternatives, guiding the transition to safer chemicals, materials and processes and reducing the potential for regrettable substitutions. This is similar to the planning approach that is central to cleaner production and pollution prevention. The six general steps for alternatives assessments are shown in Table 5.2. Alternatives assessments may include modifications to how a product is engineered or used or explore non-chemical alternatives, thereby shifting the focus from problem analysis to innovations and solutions (Geiser *et al.* 2015).

Alternatives assessment can be less or more complex, depending on the technical capacity of the user. For example, the United States Occupational Safety and Health Administration created a “Transitioning to Safer Chemicals” website and capacity training to support small and medium-sized enterprises (SMEs) in making informed choices about chemical alternatives. The goal was to instil systematic thinking about alternatives at the firm level in a relatively simple manner, providing resources for firms to make

informed decisions and understand potential trade-offs in choices (US OSHA n.d.).



There is little documentation on policy experience with alternatives assessment or with substitution. This makes drawing general conclusions on best practices a challenge, and may reflect hesitation by corporations to share potentially proprietary chemical information (Tickner and Jacobs 2016). The EU Substitution Portal SUBSPORT (SUBSPORT n.d.) and the OECD Substitution and Alternatives Assessment Toolbox (OECD n.d.) present experiences with chemical substitutions that are publicly available. These initiatives are a good basis for the collection of further experiences.

Frameworks for alternatives assessment

How potential alternatives are identified, screened for and evaluated in an alternatives assessment is guided by the choice of the framework followed. In this context a framework can be considered as the linear – and sometimes iterative – steps recommended to guide the implementation of an alternatives assessment. As discussed in a recent

review of alternatives assessment frameworks published during the last two decades (Jacobs *et al.* 2015; OECD n.d.), some frameworks are issued by regulatory authorities, such as the ECHA and the State of California, and need to be followed if the alternatives assessment is being conducted for compliance purposes. Other frameworks are primarily guidance documents developed to better inform voluntary or regulatory assessment efforts. Some frameworks are more comprehensive than others regarding suggested methods and the attributes included (including toxicological endpoints and life cycle considerations); however, the majority follow the basic structure outlined in Table 5.2 (Jacobs *et al.* 2015).

All the alternatives assessment frameworks identified share a common purpose, namely to identify a safer alternative based on a comparative assessment of hazard characteristics as well as technical and economic feasibility (Geiser *et al.* 2015; Jacobs *et al.* 2015). These frameworks require greater consistency in the methods used, as well as in the minimum steps and the level of types of data required. Consistent methods and data requirements will help support transferability of assessments from one region to another; they will also strengthen alternatives assessment as a preferred approach to addressing problem chemicals (Jacobs *et al.* 2015). However, the field of alternatives assessment is young. Gaps in methodologies, and a lack of consistent standardization and understanding of best practices across regions, can hinder global actions towards effective substitution (Tickner *et al.* 2018). To understand challenges and success factors, capacity building needs and best practices, there is an urgent need for case studies of alternatives assessment, and of informed substitution/adoption experiences in a variety of contexts (e.g. small businesses, agriculture, institutional settings and large manufacturing companies).

Common principles and criteria

Experts have noted that flexibility in the choice of an alternatives assessment framework is useful, as the substitution context can vary greatly, for example depending on toxicological assessment

capacity (Geiser *et al.* 2015). However, increased consistency and standardization are necessary in the alternatives assessment field (Jacobs *et al.* 2015; Tickner *et al.* 2018). At the international level governments and other stakeholders could establish clearer, consistent criteria for safer and less-safe chemicals and provide guidance on minimum and preferred components and attributes to be included in an alternatives assessment, creating a means to evaluate the comprehensiveness and quality of assessments. In addition, criteria for efficacy testing of non-chemical alternatives would be important in regard to substituting harmful chemicals by non-chemical alternatives. Such criteria still need to be developed.

Data gaps (e.g. on chemical identity in a formulation, toxicity, end-of-life) are a persistent challenge for alternatives assessment (Tickner *et al.* 2018). Rather than ignoring data gaps, some alternatives assessment methods make data gaps explicit or eliminate data-poor alternatives from consideration, which allows more transparent decisions and helps identify research needs. For example, in the hazard assessment component of an alternatives assessment, the GreenScreen® hazard assessment method that is used in multiple alternatives assessment frameworks has a “data gap” classification for endpoints where there is insufficient information to assess the hazard (Clean Production Action 2017). This classification is considered in the overall gradings (“benchmarks” in the GreenScreen® method), often resulting in a lower overall score (i.e. more cautious about hazard).

As in risk assessment, transparency in the assumptions made and how data gaps are addressed is essential to alternatives assessment, allowing stakeholder discussion about the best means to address a particular chemical function. The iterative process and the continuous improvement nature of alternatives assessment require periodic updating of assessments as new information becomes available.

Despite the number of alternatives assessment frameworks available, the variety of decision contexts under which alternatives assessments occur and the ever-present issue of data gaps,

the process can ultimately be guided by the Commons Principles for Alternatives Assessment (Toxics Use Reduction Institute [TURI] 2013). These Principles (to which the names of a diverse group of over 100 signatories from academia, industry and the NGO community are attached) have been designed to guide a process for well-informed decision-making that supports the successful phase-out of hazardous products, the phase-in of safer substitutes, and the elimination of hazardous chemicals where possible. The Commons Principles are: reduce hazard; minimize exposure; use the best available information; require disclosure and transparency; resolve trade-offs; and take action.

The need to consider all three dimensions of sustainable development and life cycle aspects

A yet broader approach is essential when carrying out alternatives assessments, thereby giving attention to all three dimensions of sustainable development. Taking holistic account of social, environmental and economic considerations when evaluating potential alternatives can help identify trade-offs that might occur during the life cycle of a chemical or product as a result

of substitution. The case of dental amalgam illustrates the challenges associated with the dimensions to be considered in substitution (Box 5.1).

Life cycle thinking (LCT) and, where needed, life cycle assessment (LCA) can be important components of risk management, particularly for chemical-to-process or material substitutions in alternatives assessment. LCA is a valuable tool to accompany alternatives assessment. Its efficient and effective implementation can drive innovation and diffusion of safer alternatives (Sinsheimer 2010) and identify potential trade-offs to be addressed. A life cycle approach identifies the stages of a product over its entire life cycle and potential environmental, social and economic impacts. These include raw material extraction and energy transformation through production, packaging, distribution, use, maintenance, and eventually recycling, reuse, recovery or final disposal at the end of life. LCT enables product designers, service providers, government agencies and individuals to make choices for the longer term with consideration of all environmental impacts. UN Environment hosts a Life Cycle Initiative (UNEP 2017).

Box 5.1 Dental amalgam – informed substitution in developing countries (UNEP and WHO 2014; UNEP 2016; Fisher *et al.* 2018)

Dental amalgam is a combination of metals with around 50 per cent mercury. It has been used for dental restoration during the last 150 years because of its mechanical properties and dentists' long-term familiarity with its use. Amalgam can also be a source of mercury pollution, particularly in municipal wastewater. Nevertheless, it is cheaper than other solutions for patients in many countries and has advantages compared with some alternatives (e.g. composite, glass ionomer, compomer and ceramic). Insufficient systematic studies have been undertaken regarding the ecotoxicity, as well as broader social and economic issues, related to various alternatives. Adding to this complexity, local conditions in developing countries may make the replacement of amalgam challenging, for example due to lack of a reliable water and electricity supply, which is needed when using resin-based composites (Fisher *et al.* 2018).

Many countries are phasing down (rather than phasing out) the use of amalgam, applying a stepwise and gradual approach as called for by the Minamata Convention on Mercury. This approach was taken during the East Africa Dental Amalgam Phase Down Project, which was implemented in Kenya, Tanzania and Uganda. That project included the involvement of (and consultations with) dentists and dental associations, implementation of awareness-raising activities for patients and doctors, modification of existing regulations, and improvement of dental insurance schemes. As foreseen in the Minamata Convention, measures to phase down the use of amalgam need to be multi-faceted, including setting national objectives aimed at dental caries prevention to reduce the need for dental restoration; training of dental professionals; and encouraging insurance policies that favour the use of alternatives.



© David DeKunder, Department head and research dentist, demonstrates how an amalgam separator is attached to a dental chair and how it works in removing amalgam waste to prevent it from going into the wastewater system.

In California, the Department of Toxic Substances Control requires that LCA tools be taken into account in evaluating potential alternatives. In this context, it is suggested that such an evaluation would build on an alternatives assessment and include identification of the life cycle attributes of potential concern (California DTSC 2009). These could include critical trade-offs between various alternatives and weighing the importance of different chemical attributes (e.g. cancer vs. endocrine disruption) and criteria (e.g. health vs. cost) as considerations in determining the best alternatives (Sinsheimer 2010).

There are a number of practical challenges related to the full application of LCA in alternatives assessment, (e.g. concerning data availability), while a number of methodological issues require attention (Fantke and Ernstoff 2018). The robust, sustainable and credible use of LCA needs to avoid over-interpretation of LCA results without proper consideration of its gaps and limitations. Challenges and gaps in the methodology

represent research needs for the scientific LCA community that could inspire further progress in method development (Finkbeiner *et al.* 2014). When conducting alternatives assessment, experts have recommended targeting those life cycle stages and impact categories that are comparatively different for the chemical of concern and the alternatives being considered in order to streamline and target LCA needs in the assessment (Tickner *et al.* 2018).

5.3 Strengths and weaknesses of existing alternatives assessment approaches

Informed substitution is an efficient and effective means of managing chemical risks

The process of “functional substitution” also reorients chemicals management approaches from time-intensive risk assessment, and

risk management based on single chemical substances, to comparative evaluations of the best options to fulfil a specific function. This includes considering the necessity (or technical requirements) for the function in the first place. While the concept of function may not be a key consideration in chemicals assessment and management today, chemists and designers regularly focus on function when identifying cost-effective, high-performing options for a particular product or manufacturing process (Tickner *et al.* 2015).

Substituting hazardous chemicals with safer alternatives reduces the need for complex engineering controls, safety systems, personal

protective equipment, and collection and monitoring schemes that can be costly and have the potential to fail. However, despite the fact that informed substitution supports efficient risk management strategies, an alternatives assessment is not often included within the structure of typical governmental risk management programmes (Tickner *et al.* 2013).

Substitution as an innovation driver

Framing substitution as an issue of innovation, rather than compliance, could help to scale up the application of substitution (ECHA 2018). Chemical substitution efforts often focus on removing the chemical of concern, but not on the transition

Box 5.2 Proactive substitution by frontrunners: safer alternatives for brominated flame retardants in the electronics sector (Wendschlag 2015)

Hewlett Packard (HP) is among the companies in the electronics sector that face continued regulatory and consumer pressure to remove hazardous substances of concern from electronic and electrical products. Brominated flame retardants are one class of toxic chemicals in electronics that carries risk across all product life cycle stages: during production, use and disposal. They are among the six substances restricted under the EU RoHS (Restriction of the Use of Certain Hazardous Substances in Electrical and Electronic Equipment) Directive, and also regulated under the Stockholm Convention. The increasing number of regulations and standards around the world that cover the electronics industry stimulated HP to evolve its chemical substitution approach.

To identify safer alternatives, HP created its Integrated Alternatives Assessment Protocol, which uses tools such as GreenScreen[®] to comprehensively assess the hazard profile of potential alternatives, as well as life cycle assessment tools to address the broader range of potential life cycle impacts. In its evaluation of 45 potential substitutes, HP identified roughly a dozen safer alternatives and subsequently worked with its suppliers to incorporate these substitutes into its products.

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bpa free

Table 5.3 Examples in the literature referring to potential regrettable substitution (Siddiqi, Laessig and Reed 2003; US CDC 2008; Birnbaum and Bergman 2010; US NTP 2011; Ichihara *et al.* 2012; ECHA 2013; Tomar, Budroe and Cendak 2013; Eladak *et al.* 2015; Rochester and Bolden 2015; Canadian Centre for Occupational Health and Safety 2017; Anastas, Constable and Jiménez-González 2018; Jamarani *et al.* 2018; Sackmann *et al.* 2018)

Chemical of concern (function)	Hazard of chemical of concern	Substitute	Hazard of substitute
BPA (used in production of plastics)	Endocrine disruption	BPS, Bisphenol F	Endocrine activity
DEHP (plasticizer)	Endocrine disruption	Diisononyl phthalate	Carcinogenicity, possible endocrine disruption
Methylene chloride (solvent carrier in adhesives)	Acute toxicity, carcinogenicity	1-Bromopropane (nPB)	Carcinogenicity, neurotoxicity
Methylene chloride (brake cleaners)	Acute toxicity, carcinogenicity	n-Hexane	Neurotoxicity
Polybrominated diphenyl ethers (flame retardant)	Persistence, neurotoxicity, reproductive toxicity, carcinogenicity (penta and deca)	Tris (2,3-dibromopropyl) phosphate	Carcinogenicity, aquatic toxicity
TCE (metal degreasing)	Carcinogenicity	nPB	Neurotoxicity, carcinogenicity

to safer chemistry or technologies. Redefining substitution as potential for innovation – rather than as a tool for removing and replacing problem chemicals – is therefore critical to the development of technologies that will help mitigate the current problem of toxic chemicals in the global chemical supply chain (Box 5.2).

Insufficient evaluation of potential alternatives may result in regrettable substitutions

Chemical substitution without adequate consideration of the function of the chemical, and the advantages and disadvantages of alternatives for meeting that function, can result in a regrettable substitution. A regrettable substitution is one in which the alternative turns out either to have an unexpected hazard that results in similar or worse toxicity than the chemical of concern, or to involve shifting the burden of a hazard to another entity. For example, an alternative may no longer be carcinogenic compared to the chemical of concern, but be toxic to aquatic organisms. Alternatives assessments are an attempt to reduce the likelihood of regrettable substitutions by ensuring that hazards and exposure potential are considered alongside issues of performance

and cost (Hogue 2013). Substitution should clearly take place when safer alternatives exist; it could also be the case, however, that alternatives are not totally harmless. A shift can be made to a safer alternative at the same time that research continues to find an even safer alternative solution.

Examples of regrettable substitutes include the replacement of polybrominated diphenyl ethers with tris (2,3-dibromopropyl) phosphate (TDBPP or brominated “Tris”) (Siddiqi, Laessig and Reed 2003; Birnbaum and Bergman 2010); the replacement of bisphenol A with bisphenol S (Eladak *et al.* 2015; Harney *et al.* 2003; Rochester and Bolden 2015); and the replacement of trichloroethylene and methylene chloride with 1-bromopropane (Chao and Henshaw 2003; US CDC 2008; US NTP 2011; Ichihara *et al.* 2012) (Table 5.3).

Conducting an alternatives assessment will not completely eliminate the potential for adopting alternatives that could negatively affect human health or the environment. However, concerns about problematic substitutions or missing data – or fear of “paralysis by analysis” – should not be used as a reason not to substitute. Taking

Box 5.3 Replacing highly hazardous pesticides through Integrated Pest Management and non-chemical alternatives



© Simon Kovacic/Shutterstock, Gardening with circular planting beds, a typical feature of permaculture

A number of countries have undertaken successful initiatives to reduce the use of highly hazardous pesticides (HHPs) by relying on Integrated Pest Management (IPM), an ecosystem approach to crop production and protection that combines different management strategies and practices to grow healthy crops and minimize the use of pesticides, including through the use of non-chemical alternatives.

One success story is Cuba. Eliminating the use of a pesticide was not seen as a simple substitution of inputs; instead changes in the management of agroecosystems have been introduced. This has included the use of biological agents, cultural changes, and focused application of other pesticides to phase out endosulfan (González 2016). The case of Cuba illustrates the concept of a broader functional approach where a non-chemical alternative as part of a broader IPM approach provides an alternative. Endosulfan has been used as insecticide on a global scale for vegetable and fruit crops, vineyards, cereals, coffee, tea, tobacco and cotton, among others. This HHP has caused fatal poisonings, accumulates in the fatty tissues of humans and animals and in breast milk, and is a possible endocrine disruptor. Endosulfan is included in Annex A (Elimination) of the Stockholm Convention and in the Rotterdam Convention. When endosulfan was listed under the Stockholm Convention in 2011, the Conference of the Parties (COP) asked the POPs Review Committee to assess both chemical and non-chemical alternatives. On the basis of this assessment, the Committee recommended, and the following (sixth) COP in 2013 endorsed, the recommendation that when replacing endosulfan, priority should be given to ecosystem-based approaches to pest control (Persistent Organic Pollutants Review Committee 2012; Secretariat of the Stockholm Convention on Persistent Organic Pollutants 2013).

IPM also provided the basis for a successful effort in the context of a SAICM Quick Start Programme project to phase out HHPs in Costa Rica and replace it with alternative pest management options, with a preference for non-chemical methods. Among others, the project found that there was no significant difference in roundworms infestation in pineapple production when using safer, non-chemical methods (such as commercial biopesticides and “wood vinegar”) as opposed to HHPs, while at the same time harmful side effects were reduced. As regards coffee production, trials found the combination of one or more non-chemical alternatives with reduced-rate application of non-HHP fungicides to be a feasible and affordable option (Pesticide Action Network UK 2017).

a broader functional substitution approach by considering non-chemical alternatives can provide effective means of avoiding regrettable substitutions that could occur as a result of chemical-by-chemical drop-in substitution approaches (Table 5.3).

The conventional pesticide industry and market have undergone major changes in recent decades, resulting in greater efficiency of pesticide use than in the past through major improvements to pest management technology and practices in the context of IPM programmes. In this context, biopesticides (natural materials derived from animals, plants, bacteria and certain minerals) are used in pest control. Currently, biopesticides account for 5 per cent of the total crop protection market globally with a value of about US dollars 3 billion (Damalas and Koutroubas 2018). An extensive overview of the specific uses of biopesticides can be found in the publication *Integrated Pest Management: Working with Nature* (International Organisation for Biological Control, International Biocontrol Manufacturers Association and Pesticide Action Network 2015).

Data gaps and limited experience continue to present challenges

There are a number of challenges to both the robust assessment of alternatives and informed substitution. They include gaps in chemical toxicity data, especially for mixtures such as formulated products; in data on potential exposure trade-offs; and in data on the performance of alternatives (Tickner *et al.* 2018). Furthermore, there is a need for more efficient methods and tools to assess economic and technical feasibility, as well as life cycle considerations of substitutes (Jacobs *et al.* 2015; Tickner *et al.* 2018). Toxicity and exposure gaps can be filled to some degree through the development of databases and tools that provide easy-to-access, actionable data and allow users to model missing data. Examples include the OECD's eChemPortal (OECD 2018), the US EPA's Chemistry Dashboard (US EPA 2018) and the Chemical Hazard Data Commons (Data Commons n.d.). Information on tools and potential alternatives can be accessed through

databases including the OECD's Substitution and Alternatives Assessment Toolbox (OECD n.d.), the United States Occupational Safety and Health Administration's Transitioning to Safer Chemicals Database (US OSHA n.d.) and the SUBSPORT database (SUBSPORT n.d.).

While it is acknowledged that alternatives assessment and substitution processes imply a certain complexity, it should also be noted that the level of complexity of the assessment and the attributes addressed need to fit the purpose of the assessment (Geiser *et al.* 2015; Tickner *et al.* 2018). Providing flexible guidance and best practices to help manage the complexity and uncertainties in the process will support the engagement of companies, particularly SMEs, in this field. Driven by government policies and market demands, over the past decade researchers and practitioners have developed a variety of methods and tools to assist in evaluating chemical hazards and identifying safer substitutes. Government authorities, academic institutions and NGOs have developed different alternatives assessment frameworks and tools to aid in identifying, evaluating and implementing safer substitutes (Jacobs *et al.* 2015).

5.4 Both regulatory and non-regulatory policies are needed

Policies with provisions for alternatives assessment or substitution

A review of national and international policies identified over 20 policies that include provisions for substitution (Tickner *et al.* 2013). According to available information, however, few such policies exist outside the EU and North America (Table 5.4). Three policy contexts are addressed in Table 5.4: international treaties (including consideration of alternatives evaluation); national or regional regulatory actions (including regulatory provisions specific to alternatives assessment); and non-regulatory initiatives which address substitution.

In Australia, New Zealand, and many countries in Asia and South America the implementation

Table 5.4 Examples of treaties, regulatory actions and non-regulatory initiatives with provisions for alternatives assessment or substitution (Tickner *et al.* 2013; SUBSPORT n.d.)

Component	What it involves
International treaties which include consideration of alternatives evaluation	<ul style="list-style-type: none"> › 1987 Montreal Protocol on Substances that Deplete the Ozone Layer (and amendments) › 1998 Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade › 2001 Stockholm Convention on Persistent Organic Pollutants (and amendments) (includes substitution requirements but no details on alternatives evaluation) › 2013 Minamata Convention on Mercury
Regulatory actions which include regulatory provisions specific to alternatives assessment	<ul style="list-style-type: none"> › China: 2002 Law of the People's Republic of China on the Promotion of Clean Production › China: 2006 Management Methods for Controlling Pollution Caused by Electronic Information Products Regulation › European Commission: 2002 Restriction of Hazardous Substances Directive › European Commission: 2004 Carcinogens or Mutagens at Work Directive › European Commission: 2006 Registration, Evaluation, Authorisation and Restriction of Chemicals › European Commission: 2008 Classification, Labelling and Packaging of Substances and Mixtures (CLP Regulation) (requirements for use of safer alternatives in procurement) › European Commission: 2008 Integrated Pollution Prevention Control Directive › European Commission: 2000 End-of-Life Vehicles Directive › EU: Biocidal Products Regulation [(EU)528/2012] (classification-based substitution requirements) › Japan: 1991 Law for Promotion of Effective Utilization of Resources in Japan, and 2008 mandatory industry standard (JIS C 0950, "marking for presence" of specific chemical substances for electrical and electronic equipment) › Norway: Norwegian Environmental Agency's 1976 Norwegian Product Control Act, Section 3A (pollution prevention) › Republic of Korea: 2007 Act for Resource Recycling of Electrical and Electronic Equipment and Vehicles (known as Korea RoHS) › United States: Federal Executive Order 13514, 2009: Federal Leadership in Environmental, Energy, and Economic Performance (single or multiple chemical restrictions with alternatives assessment requirements)
Non-regulatory initiatives which address substitution	<ul style="list-style-type: none"> › China: State Recommended Catalogue of Alternatives Materials for Toxic and Hazardous Substances and Products › European Commission: DG Environment's Non-Toxic Environment Initiative – 7th Environmental Action Programme › Sweden: Swedish Chemicals Agency (KEMI) Environmental Quality Objectives, "A Non-Toxic Environment" › United States Environmental Protection Agency (EPA) Safer Choice Program › United States Occupational Safety and Health Administration (OSHA) Transitioning to Safer Chemicals

of international treaties drives national programmes to use substitution as a chemical management option. Although these policies demonstrate the inclusion of substitution in various chemical management approaches, only a small fraction include specific provisions related to alternatives assessment (Tickner *et al.* 2013). Notable examples include the authorization and restriction requirements under REACH in the EU, and Safer Consumer Products regulation in the State of California (ECHA 2011; California DTSC 2012; ECHA 2014).

Although many firms may substitute in response to regulations, technical or institutional barriers can inhibit the adoption of safer technologies. Experience suggests that a multi-pronged approach consisting of incentives and disincentives is needed to achieve the goals of informed substitution (Tickner and Jacobs 2016). This approach includes requirements for alternatives assessment of chemicals of concern, as well as support structures that facilitate adoption of safer alternatives. Regulation is necessary, but insufficient on its own to drive

Box 5.4 The mix of regulatory and non-regulatory policies to support informed substitution (Ashford 2013)

Regulatory:

- › restrictions/limits on chemicals and chemical classes of concern;
- › requirements for alternatives assessment with clear guidance and enforcement; and
- › information collection requirements on chemical toxicity, uses/functions, and classification.

Supportive:

- › training for government and industry on alternatives assessment processes and informed substitution;
- › technical support networks and funding for evaluation/testing of alternatives and adoption support;
- › databases of alternatives, chemical toxicity;
- › demonstration sites, supply chain convening, and case examples of successful implementation; and
- › recognition of safer substitutes.

informed substitution and the use of alternatives assessment (Ashford 2013; Tickner *et al.* 2013). Regulations that restrict the use or trade of certain chemicals (or make those chemicals unacceptable in the marketplace) can lead to chemical de-selection (eliminating the chemical from a product or process without consideration of alternatives). The right mix of regulatory and non-regulatory (supportive) policies is essential to support innovation and substitution (Box 5.4).

Evaluations of past efforts suggest that institutional capacity within firms, to more effectively evaluate and adopt safer alternatives to hazardous chemicals, can be enhanced through incentives-based government initiatives that include research and evaluation support, guidance, information on alternatives, demonstration projects, technical assistance, databases, training, and assistance for supply chain networking of firms (Ashford 2013; Tickner



Box 5.5 The importance of policies that include technical support structures: chlorinated solvent substitution (Jacobs *et al.* 2014; US NRC 2014; Office of Technical Assistance and Technology 2015; TURI 2017)

Trichlorethylene (TCE) is a commonly used chlorinated solvent that is carcinogenic to humans (Group 1) according to the IARC and one of the most common contaminants found in hazardous waste sites in the United States. In the State of Massachusetts, under the Toxics Use Reduction Act, companies using listed toxic substances are required to annually quantify the use and emissions/waste of these chemicals and conduct an assessment of alternatives to reduce the use of the chemical every two years. With technical and research support from the Massachusetts Toxics Use Reduction Institute (TURI), funded by a small fee on chemicals, manufacturers using TCE in degreasing metal parts and other applications were able to evaluate and implement safer, water-based alternatives, reducing use of this chemical by some 95 per cent in the state and saving companies money. The TCE case in Massachusetts demonstrates the critical importance of research and technical support in overcoming technical barriers to substitution. To avoid potentially problematic solvent substitutes, a functional substitution approach to solvents as a class would be helpful.

and Jacobs 2016). For example, experience in the United States shows that toxics use reduction policies which promote substitution are more effective when supplemented with technical support structures to facilitate adoption (Box 5.5). Allowing companies degrees of flexibility in how they evaluate and adopt alternatives may lead to better outcomes and therefore more substitution. If incentive-based approaches are not successful in achieving stakeholder buy-in and cooperation, regulatory frameworks can be explored and implemented.

The roles of governments and industry

Policies can help clarify the appropriate roles of government, industry and other stakeholders in alternatives assessment and substitution processes. In developing and implementing actions, balancing the appropriate roles of government, industry and other stakeholders (given their various resources, skills and strengths) is essential. Providing certainty regarding existing and potential future regulatory requirements for chemicals is a critical element in the decision-making process of companies.

Similarly to risk assessment, alternatives assessment and substitution can be time- and resource- intensive and context/application-dependent. Unlike risk assessment, which relies primarily on hazard and exposure data, alternatives assessment requires information on functional and application requirements,

manufacturing and use conditions, performance and cost. Informed substitution is focused on the practical adoption of solutions. Experience indicates that companies and those using chemicals subject to alternatives assessment are often better situated to evaluate alternatives for their particular application in ways that can most effectively lead to the implementation of safer substitutes in their processes and products (EC 2017). Companies and users of chemicals are responsible for understanding the chemicals they are using (function/uses, toxicity, potential exposures); establishing processes to systematically and thoughtfully evaluate and adopt alternatives, involving workers, communities and supply chain stakeholders as necessary; evaluating implementation for potential trade-offs and improvement opportunities; and transparently presenting results and decisions. Companies may have to reach out to their supply chains to better understand ingredients in an article or formulation and use conditions.

Governments have an important role to play in establishing the mandates for alternatives assessment and substitution; developing criteria for chemicals and materials to avoid in substitution processes (e.g. less-safe and safer chemicals); establishing clear guidance and requirements for the alternatives assessment process; and developing metrics and the means of enforcement to monitor the substitution process. Governments can also establish non-regulatory

mechanisms that help achieve programme goals and accountability by: providing actionable data on hazard and exposure trade-offs to inform alternatives assessment; providing guidance, technical and research support and incentives for substitution; providing clear, consistent signals to the marketplace so that early actions can take place; and convening societal stakeholders. When a chemical is identified as being of concern, both industry and government are responsible for ensuring that adequate processes are in place to support the transition to safer alternatives. They may need to convene representatives across sometimes very deep and complicated supply chains and users.

There may be instances where government-conducted alternatives assessments can support industry actions (e.g. in the case of priority chemicals or sectors where there is societal demand for policy changes, or existing debate around the availability of alternatives for a particular substance). For example, the US EPA's Design for the Environment programmes (US EPA 2017) have undertaken alternatives assessments for several high-profile chemicals and applications, such as various flame retardants. The assessments required significant time, resources and stakeholder engagement. This experience suggests that while only a small number of such government-led assessments could be undertaken, they might have a large impact in driving the transition to safer alternatives by providing baseline analysis to inform industry decision-making. Greater certainty with respect to existing and potential future regulatory requirements on chemicals is a critical element in the decision-making process of companies.

Given the variety of approaches that countries and businesses have used to implement alternatives assessment, a growing amount of expertise and experience is being generated from past and present alternatives assessments and substitution cases. Governments can play an important role in establishing systematic efforts to collect and compile relevant case examples and lessons learned that can serve as a critical source of knowledge to identify and address common challenges; identify and share good

practices and success stories; and make the business case for substitution. An example is a recent report developed by the Regional Activity Centre for Sustainable Consumption and Production (Weber *et al.* 2018), which provides a number of case studies illustrating the replacement of toxic chemicals with safe and innovative alternatives. In a Canadian "combined government discussion paper and science committee report on informed substitution" a review is provided of opportunities to support informed substitution, comparative chemical hazard evaluation tools which are available, and the use that can be made of existing data (Government of Canada 2018).

Stakeholder engagement and harmonized methodologies are needed

Stakeholder engagement and collaboration are critical to address gaps in alternatives assessment methods and support the ultimate adoption of safer alternatives. For example, workers often have important information on a production process or potential exposures. They are also the ones who will be implementing an alternative (which may include changes in work processes). Adoption will be more effective if those using an alternative are involved. Actors along the supply chain, from chemical suppliers to product manufacturers to retailers, can share important information on customer needs, options that might be available and how an alternative might impact product quality, as well as information that would help to understand potential trade-offs. Stakeholder engagement helps ensure critical questions are asked during the assessment process to ensure the assessment is sufficiently complete and that implementation of substitutes occurs in an efficient manner, guaranteeing greater adoption.

During the assessment process, capacity building and greater coordination among stakeholders would help build the consistent application of alternatives assessment globally and to maintain some degree of flexibility in the methods used to support different substitution contexts. Capacity building programmes, such as the UNIDO and UNEP National Cleaner Production Centres and Networks, which can enhance working knowledge

Box 5.6 Substitution of methyl bromide: the importance of having a range of alternatives and stakeholder engagement (UNEP 2014)

Under the Montreal Protocol there has been a global phase-out of the use of controlled methyl bromide (MeBr), a powerful ozone depleter and human health toxicant linked to prostate and other cancers. For decades methyl bromide was the preferred soil fumigant for controlling a range of pests and pathogens in soil, among other uses. The search for suitable alternatives revealed that no single alternative was effective for all uses. Identification of alternatives needed to be addressed on a case-by-case basis, depending on the specific needs of the end user, regional or climactic differences, and economic feasibility. In many cases a combination of different alternatives, including chemical pesticides and non-chemical options such as steam sterilization and IPM techniques, was identified as the best approach for substitution.

There is a need for support and enforcement structures to accompany substitution programmes. Many alternatives to the use of methyl bromide, such as IPM, are knowledge-intensive. They require a broad understanding of alternative agricultural practices, as well as access to information on technological developments and improved farming techniques. Engagement and training of stakeholders, provision of technical assistance, and adaption of alternative technologies to local conditions are therefore crucial to successful substitution.

of alternatives assessment and substitution, are available to all interested parties (UNIDO 2018). Stakeholder engagement is equally important in some contexts in understanding the availability and functionality of the range of alternatives which can be used, depending on the specific circumstances (Box 5.6).

Transitioning to safer chemicals in countries with limited resources requires action on several fronts

Developing countries and countries with economies in transition are confronted by several barriers with respect to supporting the informed substitution of chemicals. Even when regulatory efforts such as the implementation of international treaties are in place to guide

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substitution efforts, there are often limited resources to collect and properly dispose of the toxic materials that were replaced. Technical resources to evaluate chemical hazards, or to identify alternatives and enforce substitution requirements under international treaties, are also limited. To remove these barriers, there is a need for technical support, capacity building and case examples of successful substitutions (UNEP and WHO 2014) (Box 5.7). This does not mean that informed substitution cannot and does not happen in developing countries. However, it often requires collaboration between research institutions, governments and employers to address gaps in capacity and information. Thus, evaluating both successful and unsuccessful substitutions, and factors that lead to success or failure, and making the results publicly available are critical to ensure effective informed substitution and improve capacity in developing countries and those with economies in transition

(Intergovernmental Forum on Chemical Safety 2008).

The private sector has a critical role to play in building capacity for informed substitution in developing countries and countries with economies in transition. This includes requirements by multinational companies that are engaged in manufacturing (or that contract manufacturing), which their suppliers implement sustainable substitution policies. These companies also need to provide technical support to regional companies and government agencies so they can undertake similar activities. Start-up companies can also play an important role in developing safer substitutes in developing countries, as many of them are associated with university research resources. Strong chemicals management foundations in developing countries remain a priority and can contribute to the success of substitution programmes.

Box 5.7 Mercury-free hospitals: the importance of participatory substitution programmes and alternative technology replacements (Burgos-Hernandez 2009; WHO 2015; Health Care Without Harm 2018)

Mercury is a persistent, bioaccumulative and toxic chemical. Its global phase-out is covered under the 2013 Minamata Convention. The Minamata Convention bans new mercury mining and calls for increased controls on mercury emissions and phasing out of mercury use in many products and processes. Hospital use of mercury-containing products is significant. The World Medical Association has urged regional and national medical associations to work within their institutions to reduce their mercury use.

In 2009 a joint project led by the University of Massachusetts Lowell, in the United States, implemented mercury replacement programmes in hospitals in Mexico and Ecuador. This programme used a participatory format that vertically engaged and trained all stakeholders on the dangers of mercury. Working groups in each hospital identified mercury thermometers, which are made of glass and easily break, and mercury sphygmomanometers (blood pressure cuffs which must be filled manually with liquid mercury) as significant sources of exposure and ideal candidates for replacement. Mercury thermometers were replaced with digital fever thermometers, and mercury sphygmomanometers were replaced with aneroid sphygmomanometers which use pressurized air.

These replacements illustrate the importance of technology substitutions, where equipment that uses a toxic chemical is replaced with a non-chemical option. Relying on hospital staff to identify problem areas and implement solutions resulted in greater ownership of preventative practices, strengthened networks, and provided a structure for continued training efforts.

5.5 Potential measures to advance assessment of chemical and non-chemical alternatives

To avoid regrettable substitutions, it is important to further refine and harmonize alternatives assessment methods, based on functional substitution as well as on the exchange of lessons learned in developing and deploying alternatives. Taking into account the preceding analysis, stakeholders may wish to consider the following measures to further advance assessment of chemical and non-chemical alternatives:

- › Focusing on functional substitution, further develop and harmonize efficient methods and tools for the comparative assessment of options to replace a chemical of concern, including their economic and technical feasibility.
- › Scale up the use of (and refine) both regulatory and non-regulatory supportive instruments, including clear criteria and guidance for alternatives assessments.
- › Identify case studies on (and ensure wide availability of information about) successful and unsuccessful substitutions, as well as on factors that lead to success or failure.
- › Strengthen the applicability to alternatives assessment of existing databases of information on chemical functions, hazards, potential exposures and life cycle impacts.

6/ Chemical risk management in facilities and during production

Chapter Highlights

International efforts are under way to facilitate a paradigm shift from managing disasters to preventing them – and to better integrate chemical accidents into broader emergency planning.

Guidance on preventing, preparing for and responding to chemical accidents is available from various bodies.

Stakeholders are often not sufficiently engaged and/or informed.

To avoid future accidents, awareness-raising, sharing of lessons learned from regulatory oversight, and promotion of good practices are essential.

While SMEs face particular challenges in managing risk, they often lack knowledge and capacity. There is a need for increased oversight and collaboration in this regard.

Workers in the informal sector are particularly at risk.

Previous chapters largely focused on risk assessment and risk management decision-making, along with opportunities to accelerate these processes. This chapter provides further insights into risk management challenges during chemical production, particularly with respect to the risk of chemical accidents. It also addresses risk management in SMEs and in the informal sector. This type of risk management presents specific challenges in many developing countries.

6.1 Understanding and addressing the risks of chemical accidents

A chemical accident can be defined as the unintentional release of one or more hazardous substances that could harm human health or the environment. Chemical accidents may occur at fixed locations (e.g. factories or warehouses) or

as a result of transport, the use of pipelines and exploration activities (e.g. operation of offshore oil platforms). The continuing occurrence of chemical accidents and their negative impacts on human health and the environment (as discussed in Part I Ch. 5, 7) point to the need for stakeholders around the world, particularly industry, to scale up actions to prevent, prepare for and respond to chemical accidents. To support these actions, policy frameworks and support programmes have been put in place internationally. The Sendai Framework for Disaster Risk Reduction 2015-2030, recently adopted by UN Member States, provides an overarching context and seeks to foster a paradigm shift – from managing disasters to preventing them – through a greater focus on managing disaster risk in an integrated way. Addressing risks from chemical accidents is an important dimension of the Sendai Framework (United Nations Research Institute for Social Development [UNRISD] 2015).

Table 6.1 Selected activities of organizations engaged in addressing chemical accidents (Inter-Agency Coordination Group for Industrial and Chemical Accidents 2017, p. 7.)

Organization	Prevention	Preparedness	Response	Post-accident	Learning
OECD	Guiding Principles for Chemical Accidents, Prevention, Preparedness and Response				Major Accident Reporting System (eMARS)
UNECE	Transboundary Effects of Industrial Accidents Convention				
EU	Seveso III Directive, Civil Protection Mechanism			Environment Liability Directive	eMARS
JEU		UN Disaster Assessment and Coordination Mechanism, Flash Environmental Assessment Tool			
UN Environment	Flexible Framework, Awareness and Preparedness for Emergencies at Local Level (APELL), Responsible Production toolkit				
UNISDR	Sendai Framework for Disaster Risk Reduction 2015-2030				
WHO		International Health Regulations			Event Management System (EMS)
	Public health management of chemical incidents				
EPSC	Member network				Member network

■ Policy, no intervention
■ Intervention based
■ Regulation/legislation/convention

EPSC: European Political Strategy Centre; JEU: Joint UN Environment/UN Office for the Consideration of Humanitarian Affairs Environment Unit; UNISDR: UN Office for Disaster Relief Reduction.

Several specialized international programmes provide targeted analysis and guidance to address various aspects of addressing chemical accidents. For example, in the UNEP Flexible Framework for Addressing Chemical Accident Prevention and Preparedness governments are encouraged to develop, improve or review Chemical Accident Prevention and Preparedness (CAPP) programmes at the national level, which would include reviewing laws, regulations, policies, guidance and other instruments (UNEP 2010). Other important international initiatives include the OECD Chemical Accidents Programme; the UNECE Convention on the Transboundary Effects of Industrial Accidents (TEIA); the WHO International Health Regulations and related activities concerning the public health management of chemical incidents and emergencies; and the Organisation for the Prohibition of Chemical Weapons chemical safety and security programmes. An overview of selected programmes and guidance of international relevance was recently compiled through an activity involving several agencies

(Table 6.1) (Inter-Agency Coordination Group for Industrial and Chemical Accidents 2017).

The importance of identifying chemical hazards

Effective management of chemical accident risks requires knowledge about the presence and location of chemical hazards. Any operator whose activities involve the production, handling or storage of dangerous substances should identify the specific accident risks associated with the types of substances used and handled, the volumes present, and the processes in which they are used. This knowledge should be incorporated in practices that prevent exposure to dangerous substances and help to ensure preparedness should such exposure occur.

Government efforts to reduce chemical accident risks generally require the establishment of a chemical hazard inventory in which industrial activities associated with the use of dangerous substances (including sites, pipelines and

transport routes) are identified, stored in a database and located, ideally on a map. Some countries develop hazard rating systems that allow prioritization of different activities by level of hazard on the basis of other information, including volumes and types of dangerous substances; types of activities; distance from populated areas; compliance records; and past accident information. Several national hazard rating schemes are described in the European Commission Joint Research Centre (EC JRC) and UNECE publication on hazard rating systems in EU Member States, European Economic Area (EEA) countries and national competent authorities under the UNECE Convention on TEIA (EC JRC and UNECE 2016).

Existing CAPP legislation (e.g. the EU Seveso Directive and the United States Risk Management Plan Rule) provide useful models for the identification of hazardous operations (EC 2017; US EPA 2018). This legislation includes lists and categories of dangerous substances and the threshold quantities that indicate a certain level of hazard. UNEP's Flexible Framework and the OECD Guiding Principles for Chemical Accident Prevention, Preparedness and Response (OECD 2003) also provide implementation guidance to support countries as they begin to identify the kinds of dangerous substances present, as well as companies that might be using these substances.

Enhanced sharing of knowledge and lessons learned

Sharing lessons learned begins with establishing mechanisms for accident reporting. Each company engaged in hazardous activities should maintain a register of accidents and near misses, as well as a programme for systematic analysis and implementation of recommendations resulting from an accident. Lessons learned from the most serious accidents and near misses should be made available to other operators engaged in hazardous activities. Data are still not available on chemical accidents in many parts of the world: companies may not be investigating them, or results from accident investigations may not be shared. Furthermore, there may be no government or industry mechanism encouraging them to do so.

In some regions and industries, however, public databases that contain chemical accident information have been established. These include, notably, the EU eMARS database and various country and industry databases (e.g. ARIA, ZEMA, CSC, RIHAD) as well as the published results of investigations and studies concerning chemical accidents. eMARS is a public database containing over 900 reports of chemical accidents and near misses reported by EU, EEA, OECD and UNECE countries. Reporting major accidents to eMARS is compulsory for EU Member States when the event meets the criteria defined in Annex VI of the Seveso Directive. In the case of non-EU OECD and UNECE countries, reporting accidents to the eMARS database is voluntary but is regularly carried out (Inter-Agency Coordination Group for Industrial and Chemical Accidents 2017). Accident databases only provide information on chemical accidents that have already happened.

The probability that serious chemical accidents will occur in highly industrialized countries is generally low. In these countries only some risks are manifested as accidents during a given time period, while in other countries accidents take place more frequently (see Part I, Ch. 5). Additional research on the national and regional dimensions of chemical accidents has been carried out, including in China (He *et al.* 2011; UNEP 2011), India (Sengupta *et al.* 2015) and Africa (UNEP 2017). It suggests that when facilities that process hazardous materials are transferred from developed to developing countries, the process safety standards for such facilities which applied in the former should not be lowered, irrespective of local regulations.

Exchange networks of practitioners can be valuable sources of information on chemical accident risks, particularly for identifying ways to prevent accidents. Depending on the topic, these networks can consist of groups of experts in the same industry or the same profession; government regulators; and cross sections of experts from government, industry and academia. Such information exchange helps operators engaged in hazardous activities assess risks in order to improve their risk management strategies, while it also helps authorities prioritize hazard sources and topics for inspections. Along

with information from accidents, expert exchange can substantiate the need for modifications to technical standards, improvements to regulations, and enforcement policy regarding safety performance at installations. There are many examples of such groups in developed countries and in multinational industries, including the Center for Chemical Process Safety (CCPS), the Energy Institute, the International Association of Oil and Gas Producers, the EU Seveso Expert Group, and the OECD Working Group on Chemical Accidents. There are also many examples of exchange networks that guide the establishment of new networks in regions and industries where they are needed.

Understanding the causes of chemical accidents

Past accidents cannot directly provide information on accidents that might happen. Hence other types of information are needed in order to identify activities and practices that are likely sources of future accidents, so that measures can be taken to reduce risks before accidents occur. The information in chemical accident databases, together with the publication of the results of investigations and studies concerning these accidents, have facilitated a proliferation of studies whose purpose is to identify their causes.

Analysis of past accidents is valuable for developing insights into why accidents occur

in the chemical processing industry, together with the damage they cause. Such analysis of major chemical accidents, and the determination of required measures and communication of results, should be carried out by independent authorities. This can provide “wisdom of hindsight” to help prevent accidents or mitigate the impacts of those which nevertheless still occur (Tauseef, Abbasi and Abbasi 2011). To avoid future accidents, it is essential to share good practices and implement the recommendations in these analyses. There are ongoing efforts to improve analytical methods and to identify more effective approaches to the prevention of accidents and their consequences.

It has been shown that accidents occurring today frequently result from well-known and well-understood failures which had already been identified in the case of past accidents. Abu Bakar *et al.* (2017) reviewed 770 major accidents using four summary categories associated with the risk-based process safety (RBPS) framework. They concluded that the most common accident contributors were linked to process hazards (19 per cent), operating procedures (17 per cent) and lack of employee participation in process safety management (12 per cent). Gyenes and Wood (2014) used the seven elements of a safety management system from the 2012 EU Seveso Directive to review the causes of 86 major accidents notified to the eMARS database. They concluded that the major cause of accidents was



© Claudia Cabal, an electrical station storing PCB equipment in Paraguay following a large fire

related to deficiencies in operational control (28 per cent). Other studies have examined, for example, the roles of maintenance (Okoh and Haugen 2014) and of equipment failure (Kidam and Hurme 2013).

The study of accidents can also reveal new sources of risks associated with changing technologies and with business practices. Taylor *et al.* (2017) looked at findings from 12 industrial catastrophes, including four chemical events. They found that increasing engineered complexity, technical specialization, fragmented contractual arrangements and other factors make it increasingly difficult for individuals and organizations to recognize weaknesses in risk control. Often problems arise because current approaches to risk analysis are not able to consider adequately the influence of a vast array of relevant inputs such as leadership issues, operational attitudes and behaviours, commercial and budgetary pressures, and communication issues.

In addition, accident analysis can identify complex causality and systemic vulnerabilities resulting from the way an organization operates. As Sklet (2004) observed, experience with accidents has shown that major accidents almost never have

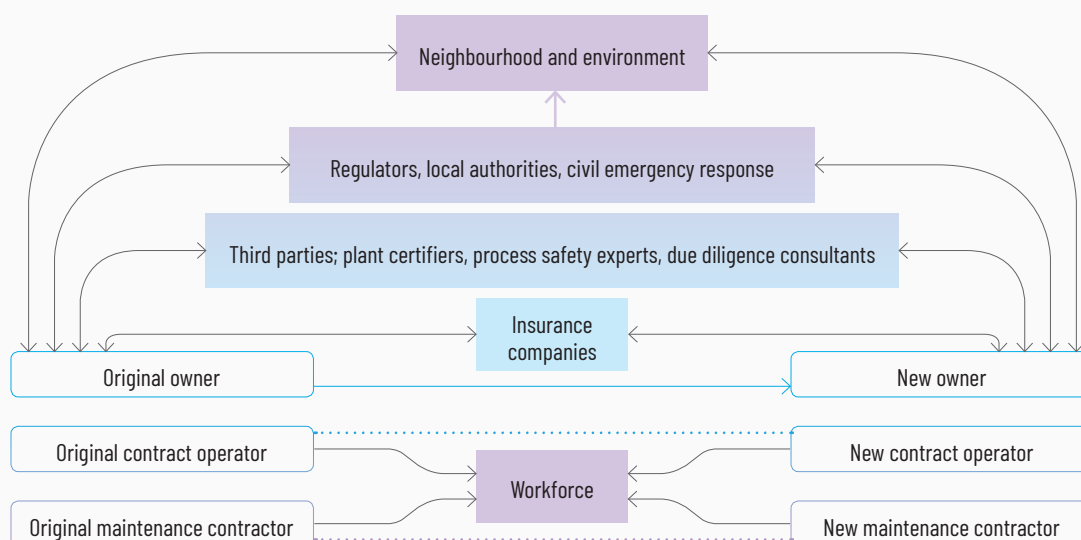
a single cause; most accidents involve multiple, inter-related causal factors. This complexity should be reflected in the accident investigation process. Various analytical techniques are available to support investigators in structuring information and focusing on the most important features.

Emerging topics of interest

Lessons emerging from recent accidents cover a spectrum of actions to ensure improved chemical accident prevention, preparedness and response. These actions range from strong engagement by senior leaders (in public authorities and companies) (OECD 2012) to addressing emerging risks associated with growing production and use of clean fuels, cybersecurity, and technological accidents caused by natural disasters.

One issue being discussed by the international community concerns possible risks that result when ownership changes. At hazardous facilities such changes of ownership are very common and can potentially affect key aspects of safety management (OECD 2018a) (Figure 6.1). Current and new owners may be specialist companies with a significant industry background, or they may be “non-specialist” companies with a more

Figure 6.1 Stakeholders in the change of ownership of hazardous facilities (adapted from OECD 2018a, p. 14)



diverse business portfolio. In certain cases, poorly managed change of ownership (including oversight responsibilities) could potentially have detrimental consequences for safety at a facility.

The death of many private and public firefighters during chemical accidents is another cause of concern. Efforts to develop emergency planning – with strong specialized training for first responders and direct cooperation with companies – should continue (OECD 2018b). Other topics emerging from recent accidents include the safety of underground gas storage; the safety of pipes and (long distance) pipelines; risks of chemical accidents in harbours; risks posed by facilities where highly active substances are handled (including high potency active pharmaceutical Ingredients and agrochemicals); the management of ageing facilities; improving clean-up and recovery and, more generally, ensuring proper safety maintenance programmes; and addressing risks arising from natural hazard triggered technological (Natech) accidents.

Natural hazard triggered technological (Natech) accidents

Natural hazards can trigger fires, explosions and toxic releases at hazardous installations and in critical infrastructure (e.g. at fixed chemical installations, in oil and gas pipelines and on offshore platforms). “Natech accidents” frequently occur in the wake of natural disasters. They often have severe long-term consequences for the population, the environment and the economy. The risk of Natech accidents is expected to grow as a result of climate change and increasing industrialization. In particular, climate change is likely to increase the frequency and severity of hydro-meteorological hazards, raising concerns about an increase in the number of Natech accidents due to storms. Preliminary studies indicate the extent of the damage severe storms can cause (Krausmann and Salzano 2017). There are currently no systematic analyses of storm-triggered Natech accidents. Nevertheless, lessons can be learned from the impact of extreme weather and climate events such as Hurricane Harvey, which caused extreme precipitation (particularly over Houston, Texas

in the United States and the surrounding area) in August 2017, resulting in extensive flooding, loss of life, high economic costs, and impacts on critical infrastructure, airports and industry (Sebastian *et al.* 2017; van Oldenborgh *et al.* 2017; Jonkman *et al.* 2018; Gori *et al.* 2018) (Box 6.1).

To address Natech accidents and manage their consequences when they do occur, targeted prevention, preparedness and response are needed (Krausmann and Salzano 2017). However, disaster risk reduction frameworks do not always consider technological hazards, while chemical accident prevention and preparedness programmes often overlook specific aspects of Natech risks. Natech risk assessment tools and guidance for industry and government authorities are therefore needed to support better Natech risk management at the national and local levels (UNISDR 2018). In addition, Natech risk assessment is an important instrument for determining where Natech risk spots exist within a region and where detailed risk assessment is required. Although the potential consequences of such accidents are understood, the cost of additional safety measures to reduce Natech risk can result in reluctance to accept that these risks exist and to act to reduce them (Girgin, Necci and Krausmann 2017). Guidance for prevention, preparedness and response to address natural hazards triggering technological accidents is available from the OECD (OECD 2015).

Commitment by senior company leaders, effective governance, and capacity development

Systematic data on the economic cost of chemical accidents are lacking, and it is often difficult to prove to senior officials that the resources spent on accident prevention pay off (OECD 2018c). If no accidents occur, less attention may continue to be paid to prevention. Yet the costs of chemical accidents, which may be significant, can affect the stock value of an affected company (Makino 2016). Efforts are ongoing to substantiate the risks and costs of chemical accidents and raise awareness about accident prevention at higher policy levels (OECD 2018c). The engagement of senior leaders of companies in understanding the risks posed by their facilities, and the importance

Box 6.1 Lessons learned from Natech accidents triggered by Hurricane Harvey (Necci, Krausmann and Girgin 2018)

Hurricane Harvey made landfall on the Gulf coast of Texas in August 2017. The lessons to be learned from the Natech accidents triggered by this storm include:

- › Preparation for past levels of storm severity is not sufficient. In view of ongoing climate change, storm frequencies and intensities could change and, with them, the associated Natech risk.
- › Although natural hazards and vulnerabilities may be known, industry does not always adequately protect its equipment from impacts. In areas where there is a known flood hazard, use of protection measures should be enforced to prevent equipment damage and the subsequent release of hazardous materials.
- › Floodwaters are a transport vector for released toxic or flammable substances, distributing them over potentially wide areas. Where there is an ignition source, devastating fires can occur which are also transported with the flood. This risk is as yet inadequately considered.
- › Current and former waste sites are vulnerable to flooding, but little has been done to mitigate the risks they pose. Such sites should be protected from flooding, and investment should be allocated to completing remediation activities as quickly as possible.
- › Significant airborne emissions can be created by flaring during facility shutdown and restart operations before and after a storm. Areas with a high density of industrial facilities should have plans to schedule restart operations in a way that does not affect air quality.

of investing in process safety, is critical in this process.

Integrating chemical accidents in emergency planning at several levels of governance helps ensure that the risks and management of chemical accidents are addressed at the community, municipal, regional and national levels in an integrated way (UNRISD 2018). Effective land use planning policy is an essential part of this integrated approach, as is the engagement of the health sector in prevention, preparedness, response and recovery (WHO 2018). Coordination across borders may be relevant in order to address the risk of transboundary accidents.

The activities described above require the development of effective risk management systems and the scaling up of capacity development efforts. At the national level, Cambodia, Mali, the Philippines, Senegal, Sri Lanka and Tanzania have prepared national roadmaps to develop CAPP programmes with support from the United Nations Environment Programme and the SAICM Quick Start Programme Trust Fund. Common priorities identified through these projects include adequate enforcement of existing regulations; drafting new legal texts to implement CAPP; establishing ongoing

coordination mechanisms; and establishing a central information management system (i.e. a database) (UNEP 2015). Given the role played by human factors in causing chemical accidents, training concerned individuals is a key aspect of capacity development for chemical accident prevention, preparedness and response. To better measure these and other capacity development efforts, a capacity development framework has been proposed to assess progress and help compare capacity levels for prevention of and preparation for chemical accidents in countries (Baranzini *et al.* 2018).

6.2 Chemical risks in developing country SMEs

6.2.1 Challenges in developing country SMEs

Use of safety data sheets

Many SMEs in developing countries routinely use and handle chemicals. When they do so, attention needs to be paid to accompanying labels and safety data sheets (SDS). Often, however, developing country SMEs carry out

their activities without having proper on-site list of hazardous substances, accompanied by corresponding SDS. Moreover, employees receive only limited training and re-training to help them understand and apply the information found on labels and SDS (Massey 2008). To be effective, communication of risks to employees needs to be simple and practical, taking into account the context and their level of education. A study in China that assessed a behaviour-based safety management approach showed that workers identified safe and unsafe practices and took part in addressing them (Yuan and Wang 2012).

In developing country SMEs a number of quality insufficiencies in the SDS system can be observed. These include the SDS frequently being incomplete or inaccurate; lacking important information about guidelines for controlling exposure; and having been created by the manufacturer and therefore possibly not having been subject to significant scrutiny by government authorities. SDS may also be inconsistent; for example, in some cases several firms sell the same chemical but the corresponding SDS are different (Massey 2008).

There are several possible reasons for the underuse or inadequacy of SDS in the SME sector. For example, those prepared by chemical

manufacturers to comply with regulations may not meet the needs of the people exposed to the chemicals; an example would be SDS in a language that workers and others who are supposed to read them cannot understand. On the other hand, SMEs that use chemicals, but have a poor understanding of the SDS, are unlikely to have much interest in trying to benefit from them.

Process safety

The Risk Based Process Safety (RBPS) approach recognizes that all hazards and risks in an operation or at a facility are not equal. Consequently, safety-related resources are attributed in a way that focuses on estimated greater hazards and higher risks. According to the Center for Chemical Process Safety (CCPS) (2017), “using the same high-intensity practices to manage every hazard is an inefficient use of limited resources. A risk-based approach reduces the potential for attributing an undue amount of resources to managing lower-risk activities, thereby freeing up resources to address higher-risk activities.”

Commitment to process safety addresses a number of key elements, including the importance of a process safety culture; strict compliance



with standards; promotion of process safety competencies; total workforce involvement; and a strong stakeholder outreach programme. Process knowledge management, coupled with hazard identification and risk analysis capability, are key elements for understanding process safety. Without risk-based process safety prioritization, it would be difficult and unaffordable for most developing country SMEs to fully address hazards and risks (Verbano, Venturini and Venturini 2013; CCPS 2017). Developing country SMEs also need more technical assistance with the design and implementation of process safety management systems.

Occupational health and safety

Many work environments in developing country SMEs are dangerous. Not only do a large share of occupational accidents in these countries occur in SMEs (Nyirendaavwil, Chinniah and Agard 2015), but chemical accidents in SMEs are seriously under-reported because of poor data and analysis capabilities. Risks therefore need to be systematically assessed, analyzed and, where necessary, reduced to improve safety at work (Nordlöf *et al.* 2017).

The adoption of a functional occupational health and safety management system (OHSMS) by an SME is an important measure that can lead to fewer occupational accidents. Regularly measuring and keeping track of a company's safety culture, and openly discussing occupational health and safety (OHS) values, are priorities in this context. Factors such as the company's size, its safety culture, the extent of high-level company commitment, lack of relevant skills, lack of technical know-how, lack of formalized routines, and financial affordability need to be understood and addressed (Nordlöf *et al.* 2017). In Malaysia, for example, although OHS regulations exist, 80 per cent of facilities investigated failed to fully comply with them (Hong, Surienty and Kee 2011). Where OHS takes a back seat to productivity, competitiveness and profitability, (complete) adoption of an OHSMS is prevented in developing country SMEs.

Access to finance for occupational health and safety management systems

The level of financial performance can be associated with occupational health and safety management (OHSM) practices, as demonstrated in a Swedish study on companies' credit worthiness. According to this study, better financial performance and better OHSM practices can reinforce one another in a positive and cyclical spiral (Nordlöf *et al.* 2017). In some countries the government provides important financial and technical assistance to support OHS implementation in SMEs. Such is the case with support provided in Malaysia by SMECorp, an agency under the Ministry of International Trade and Industry in charge of overall policies and strategies for SMEs (Hong, Surienty and Kee 2011). Similar specialized agencies are found in other countries. Sometimes National Cleaner Production Centres assume this role. An interesting approach in some countries includes partial subsidization of occupational health and safety activities. For example, in Japan and Finland half the cost is subsidized (Mizoue *et al.* 1999).

6.2.2 Improving chemical safety in developing country SMEs

Further steps in the transfer of safety technology

The incidence of occupational injuries and diseases associated with industrialization has declined markedly in highly industrialized countries as a result of the adoption of engineering controls, strict use of protective equipment, reliance on safer machinery and processes, and greater adherence to applicable regulations and labour inspections (Kim, Park and Park 2016). To improve OHS in all countries, modern legislation and consequent interventions to help improve work environments increasingly need to take account of the specific characteristics and needs of SMEs (Legg *et al.* 2015). In this respect, it is also important for advanced safety technology to be used in developing country SMEs.

Developing country SMEs need assistance in making technological changes. Facilitating transfers of safer technologies to these SMEs

would be of great importance in preventing accidents at the workplace. A crucial first step would be for these SMEs, if feasible, to replace dangerous old equipment (Yuan and Wang 2012). Besides improving OHS conditions, technology transfers could promote the sustainable development concepts of recovery, reuse and recycling. Universities and research centres can be an important source of knowledge and experience to share with SMEs in order to support their transition to better and safer technologies and practices. Bhandubanyong and Pearce (2017) identified the need for foundries in Thailand, especially in the SME sector, to receive more encouragement, guidance and support in seeking to make technical improvements in their operations, for example through better cooperation and interaction with university/government R&D centres such as the National Metals and Materials Technology Center. Similar opportunities exist in other developing countries with respect to many types of SMEs and activities.

Promoting a more proactive safety culture in SMEs

A key element of occupational safety and health management is the promotion of a culture of prevention within an enterprise (ILO 2014). Lessons from past disasters underline that it is of the highest importance to create a corporate culture in which safety is fully understood and treated as the number one priority in any business. It is clear that an occupational safety and health management system is not effective unless there is a positive safety culture in the workplace (Kim, Park and Park 2016). The characteristics of a positive safety culture include proper leadership that is highly visible and committed to safety, as well as clear communication of safety as a priority value that cannot be traded off against cost and schedule (International Atomic Energy Agency 2006; Unnikrishnan *et al.* 2015). In a developing country setting it is important to remember that many SMEs start as family businesses. In such cases, management may fail to fully understand concerns about chemical risks and occupational safety. Initiating a safety culture will therefore need to start with the engagement of management and various behavioural aspects

will need to be taken into account (Yuan and Wang 2012).

Guidance provided in the ILO Convention concerning the Promotional Framework for Occupational Safety and Health (ILO 2009) calls for an occupational safety and health management system approach. The main purpose of such a system is to pursue continual improvement in occupational safety and health performance through the use of the Plan-Do-Check-Act cycle. The Convention sets out how national policy, national systems and national programmes should be designed in order to promote continuous improvements in occupational safety and health (Kim, Park and Park 2016).

Linkages and the interaction of companies with other players in the field (e.g. through value chain linkages with global markets or through being part of a multinational company) are encouraging the introduction of voluntary standards, global environmental management and corporate social responsibility systems; sustainability reporting initiatives; and advanced product quality programmes – all of which contribute to improved environmental performance at chemical production facilities, including SMEs (He and Yang 2012).

Promotion of investments in chemical industry parks

Clustering companies creates synergies and economic benefits by providing shared access to networks, suppliers, distributors, markets, resources and support systems (Heikkilä *et al.* 2010; Reniers and Amyotte 2012). Since 2006 China has adopted a policy of relocating SMEs to chemical industry parks, rather than leaving them dispersed throughout the country. Clustering is considered to facilitate the safety and environmental supervision activities of chemical companies by park management authorities and relevant government agencies (Zhao *et al.* 2013). It is clear that collaboration between adjacent plants to prevent (internal and external) domino effects in a chemical industrial cluster can help save lives and avoid considerable costs that might arise as a result of chemical accidents (Reniers, Cuypers and Pavlova 2012)



Clustering can facilitate/incentivize materials exchange. For example, waste from one facility may be input for another. Simple practices such as materials exchange can prevent significant volumes of hazardous waste or effluents reaching waterways or soils (Massey 2005). However, realizing the OHS benefits of what are sometimes referred to as “eco-industrial parks” is proving difficult in developing countries and could be strengthened (Kultida *et al.* 2015).

Clustering companies characterized by substantial use of chemicals in a special area that provides the right infrastructure is desirable. For example, the Government of Bangladesh has decided to implement this approach with tannery SMEs in Dhaka City. Tanneries had been functioning in an unplanned manner, scattered and surrounded by populated areas and with no effluent treatment. The government therefore proposed a new location, with land dedicated to industrial plots and to a central effluent treatment plant, disposal yard, electricity sub-station and other necessary infrastructure. All tannery operations are being moved to this area. Similar initiatives could be implemented with respect to other traditional

and significant activities in developing countries, such as brick production and foundries (Paul *et al.* 2013).

6.2.3 Further research on (and knowledge about) chemical safety in SMEs is needed

Most occupational health and safety research, policy and legislation have been – and still are – skewed in favour of large enterprises (defined as those with more than 250 employees) that have the resources to influence, interact with and contribute to policy development and research (Legg *et al.* 2015). Often SMEs do not have the necessary resources (in the form of human capacity and finance) to contribute to the research, development and demonstration of the OHS practices needed to address this problem (Legg *et al.* 2015). Some characteristics of SMEs make it extremely difficult for them to create and maintain a safe and healthy work environment, or to manage effectively with respect to safety issues (Targoutzidis *et al.* 2014).

The OHS challenges of developing country SMEs need to be researched more thoroughly so as

to provide better inputs for SME policy design and legislative review. Limited information about these SMEs already shows that workers are more routinely exposed to hazardous situations and suffer more work-related injuries and illnesses than those in larger companies (Targoutzidis *et al.* 2014). Further research on the relation between injuries, accidents and the sizes of enterprises could help show how size matters in OHS management (Micheli and Cagno 2010).

6.3 Chemical risk management in the informal sector

6.3.1 Risk management challenges in the informal sector

The informal sector presents unique management challenges

The informal sector is usually characterized by small-scale activities that are not registered, taxed or monitored by any form of government authority, while the hundreds of millions of women and men who work in this sector often are poorly paid and carry out dangerous work (OECD 2002; Maiguashca 2016). More than 60 per cent the total global labour force is employed in the informal sector, and 93 per cent of informal employment is in emerging and developing countries (ILO 2018a). Despite a lack of detailed data on informal enterprises worldwide – and variations in the definitions of “informality” – it is clear that the number of these enterprises is very high and that a large share of all SMEs are in the informal sector (Charmes 2012; ILO 2015a). In Africa almost 86 per cent of employment is informal; the share is around 68 per cent in Asia and the Pacific, almost 69 per cent in the Arab States, 40 per cent in the Americas and about 25 per cent in Europe and Central Asia (ILO 2018a). People in rural areas are almost twice as likely to be in informal employment as those in urban areas: agriculture, where pesticides and other chemicals are widely and heavily used, has the highest level of informal employment, estimated at more than 90 per cent globally (ILO 2018a).

The production, consumption and disposal of chemicals can have external negative (spillover) impacts on individuals and firms outside these activities when they are not well managed. While informal and/or illegal behavior is often the source of chemicals pollution, by their nature it is unlikely that firms involved in these undertakings will take steps to internalize costs. Many such externalities can be reduced through responsible chemicals management (Hassan 2012; UNEP 2013).

A challenge for risk management in the informal sector is the lack of a clear overview of the nature, extent and location of informal activities/operations in countries. By definition, some or all aspects of informal economic activity are not included in the formal record and hence there is an information and statistics gap regarding these activities (Benjamin *et al.* 2014). This means the informal sector remains outside the scope of planned development and health and safety policies, as there is little information available to prioritize areas of prevention (Mukim 2011).

Limited knowledge about chemicals in the informal sector

Chemicals are used and handled in many informal activities in addition to agricultural ones, including cleaning, welding, construction, and employment in garages/workshops (Zock 2005; Ahmad *et al.* 2016). Informal workers are highly vulnerable to the health risks presented by the chemicals to which they are exposed daily due to poor working conditions, limited knowledge about chemical risks, high levels of exposure and lack of access to health care, among other factors (ILO 2018a; ILO 2018b; International Institute for Environment and Development 2018). Workers' level of education is important. Globally, when the level of education increases, the level of informality decreases; comparing national data on informal employment as a share of total employment with Human Development Index (HDI) values shows that countries with higher informality have a lower HDI value (ILO 2018a). The health impacts of working in informal enterprises range from skin irritation, respiratory allergies and asthma to acute poisonings, cancers

and reproductive disorders (Rongo *et al.* 2004; Rockefeller Foundation 2013). Poor practices, such as failure to use personal protective measures or smoking at the workplace, are common in the informal sector and exacerbate the risks associated with chemical use (Rongo 2005).

Workers in the informal sector lack knowledge about chemical labelling and how to understand it. Furthermore, labels may be absent (Lajini 2014; Makhonge 2014). Actors in the informal sector are, however, obviously not exempt from legal requirements in a country and could be targeted by governments for information provision and inspections.

Lack of a safety and health culture

Since low-skilled and labour-intensive work in the informal sector is performed by people with low socio-economic status, they usually show greater readiness to accept dangerous working conditions. For example, waste pickers interviewed at the Mbeuebeuss waste dump in Senegal – some of whom were women, although many more were men – indicated that they had little choice but to undertake this type of work to survive despite the health risks to which they were exposed and the difficulty of obtaining health care (Vasina 2018)

Gender inequalities

Gender inequalities and child labour are common in informal activities (UNRISD 2010; ILO 2018a). In a globalized economy, women and children increasingly participate as wage earners. Among men, a higher share is employed in the informal sector than among women, both in developing and developed countries as well as in the agricultural and non-agricultural sector (ILO 2018a). However, the picture is heavily influenced by a few highly populous countries, as in low and lower-middle income countries the share of women informally employed exceeds that of men. Moreover, as the ILO concluded in its 2018 report, women in the informal economy are more vulnerable.

A study on female horticulture workers in Tanzania illustrates the chemical risk situation in informal agriculture. Women often bring their children to the fields because they lack access to or cannot afford day care services. The elder children help with work on the farm. Women and children often work in fields where pesticides are being applied. Further exposure (and that of other family members) can occur when contaminated clothes are washed in the household or even through pesticides stored in the kitchen or bedroom (Mrema *et al.* 2017).

Informal e-waste recycling

Recycling of metals found in waste (secondary production of metals) is growing rapidly worldwide. Metals such as aluminium, copper and gold can be recovered from e-waste (or electronic and electrical equipment waste). This activity is mainly carried out in the informal sector in developing and emerging countries such as China, Ghana, Brazil and India (e.g. 95 per cent of e-waste in India is treated and processed in the informal e-waste recycling sector) (Zheng *et al.* 2016; Chakraborty *et al.* 2018).

6.3.2 Policy challenges and opportunities

Formalization

ILO Recommendation No. 204 on transition from the informal to the formal economy acknowledges that most people enter the informal economy not by choice, but because of a lack of opportunities in the formal economy and an absence of any other means of livelihood. It provides strategies and practical guidance on policies and measures to facilitate the transition from the informal to the formal economy (ILO 2015b). The formalization of informal activities can contribute to better conditions for workers and achieve more inclusive and more sustainable development. In support of formalization, government regulations for licensing and registration may need to be made simpler and more practical. Measures also need to be tailored to specific circumstances in countries and to specific economic activities. An example related to chemicals is artisanal and small-scale gold mining (Box 6.2).

Box 6.2 Formalizing artisanal and small-scale gold mining

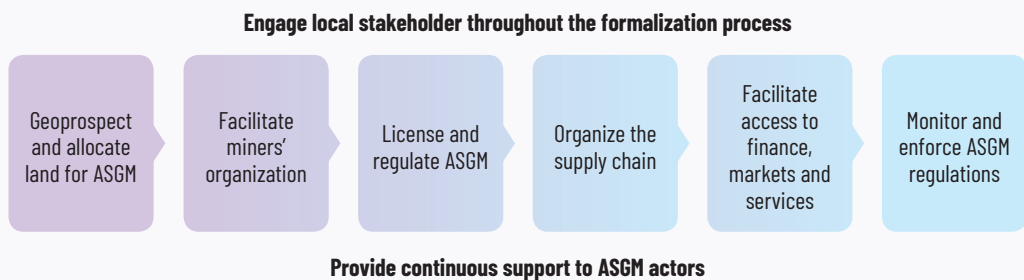
Artisanal and small-scale gold mining (ASGM) has been estimated to provide direct employment for over 16 million people (approximately one-third are women) and accounts for up to 20 per cent of the world’s gold production (Seccatore *et al.* 2014; Veiga, Angeloci-Santos and Meech 2014). Despite this sector’s importance for socio-economic development, it has negative health and environmental impacts. For example, many ASGM miners use mercury to separate gold from sediment and ore. The resulting mixture of mercury and gold, or amalgam, is heated to vaporize the mercury and leave the gold behind, harming miners and their communities and contaminating the surrounding environment.

Many of these challenges stem from the sector’s typically informal nature, which deprives ASGM miners of access to financial and technical assistance, thereby perpetuating precarious working conditions and hindering the miners from adopting more sustainable mining practices. In recognition of this, the Minamata Convention on Mercury requires Parties with “more than insignificant ASGM activity” to develop National Action Plans (NAPs) for reducing mercury use in the sector, which should include “steps to facilitate the formalization or regulation” of the ASGM sector. Formalization is a process that seeks to integrate the ASGM sector into the formal economy, society and regulatory systems (UNEP 2012). If it is undertaken in a comprehensive and inclusive manner, formalization can help to address health and environmental impacts and unlock the sector’s full development potential.

To support countries in undertaking such formalization efforts, the United Nations Institute for Training and Research and (UNITAR) and UNEP have prepared the *Handbook for Developing National ASGM Formalization Strategies within National Action Plans* (de Haan and Turner 2018). The Formalization Handbook provides a comprehensive introduction to ASGM formalization, including key concepts and terminology, key components of the formalization process, possible approaches and best practices. This is followed by step-by-step guidance for creating an enabling environment for ASGM formalization and developing a national strategy for formalizing the ASGM sector. Various issues and approaches are illustrated with case studies from developing countries. The Figure below shows the key components of the formalization process, which are discussed in detail in the Formalization Handbook.



© UNITAR/Jordan De Haan, artisanal and small scale gold miner



Extension of health insurance and other social services to workers in the informal sector

Despite the high risks they face, most Informal workers are not covered by social insurance. A number of countries have been looking at extending some form of social insurance to informal workers (ILO 1997; Thornton *et al.* 2010; Alfors 2013). With a few exceptions, most social protection policies remain gender-blind. Gender-responsive reforms could help ensure increased coverage of women, including informal workers. Not only do experiences of poverty and vulnerability differ for women and men, but women face life cycle risks that require particular attention and coverage from social insurance schemes (e.g. to reduce risks associated with childbirth). In addition, women may accept work in the informal sector while also performing paid or unpaid domestic and care work (Holmes and Scott 2016; Alfors, Lund and Moussié 2018).

Multi-stakeholder engagement to promote occupational health and safety

The involvement of a number of different stakeholders is valuable for promoting occupational health and safety (OHS) among informal workers. For example, NGOs previously involved in communities of informal workers are likely to be well aware of the context of those communities and of needs in a specific sector. Moreover, personnel from NGOs, who may be seen as leaders by certain groups, can influence behavioural change to safer practices. The media are another group that could promote awareness and sensitize workers. Clear and correct messages should be designed with the media, so that they can be delivered to informal workers in an adequate and comprehensible way (Singh *et al.* 2011).

6.4 Potential measures to further advance risk management in facilities and during production

Leadership by decision-makers, industry responsibility, collaboration of actors in the supply chain, and increasing awareness and understanding among workers are crucial to prevent chemicals-related accidents and to facilitate sound chemicals and waste management, particularly in SMEs and in the informal sector. Taking into account the preceding analysis, stakeholders may wish to consider the following measures to further advance risk management in facilities and during production:

- › Better integrate chemical accident prevention, preparedness and response into disaster risk management at all levels.
- › Improve the understanding of risks and process safety in facilities, and strengthen information and knowledge-sharing on chemical accidents globally.
- › Step up efforts to enhance access, awareness and understanding of relevant chemical hazard and safety information among workers, particularly in SMEs and in the informal sector.
- › Encourage larger companies to work with SMEs in sharing knowledge about chemical risk management.
- › Scale up capacity development measures through the supply chain in order to strengthen risk management capacity in the informal sector.

7/ Approaches to sustainability assessment

Chapter Highlights

Approaches that assess broader sustainability issues and potential trade-offs provide important complementary tools beyond assessing and managing the risks of chemicals.

Life cycle management is an approach increasingly used by companies to support more sustainability-focused supply chain risk management.

A host of life cycle assessment methods are available which allow wider sustainability assessment, and more such methods are under development.

Choices about when and how to use these methods need to be made, taking into account available capacities and resources, supply chain requirements and the regulatory context while avoiding “paralysis by analysis”.

In chemicals management the entire product life cycle has to be considered in order not only to take the human and environmental safety aspects of a chemical into account, but also to assess the wider sustainability parameters that can play a role. This chapter discusses the possible trade-offs that need to be made in this context by decision-makers and describes the tools which are available to assist them in this respect.

7.1 A holistic approach to assessing sustainability

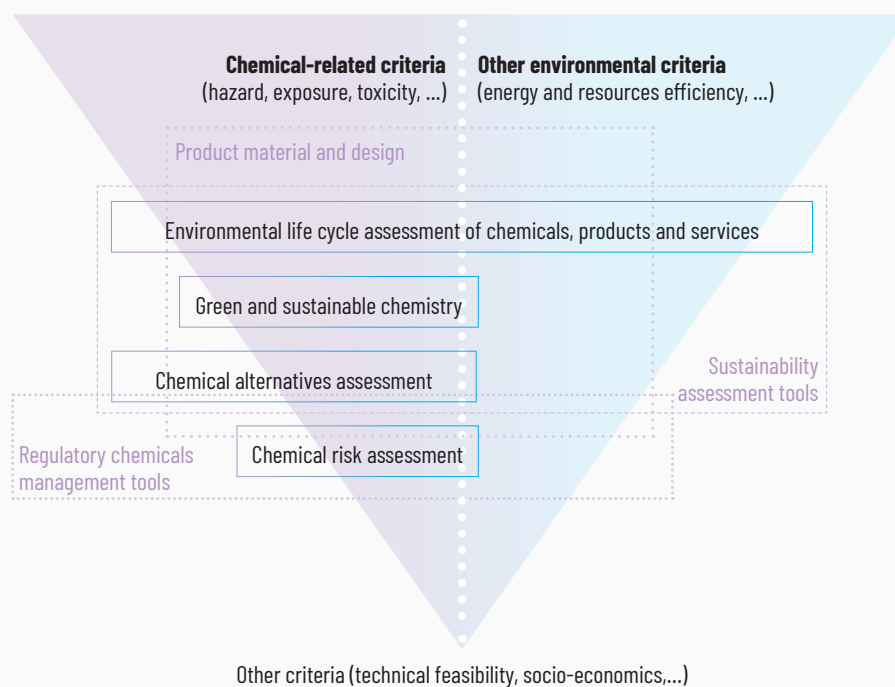
A holistic life cycle approach allows comprehensive chemicals management with respect to various dimensions of sustainability. Not only does such an approach involve the assessment and management of the direct consumer and occupational risks of (groups of) chemicals. It also combines these risks with those from chemical exposure mediated via the environment. Considering all sustainability aspects at the design stage of a chemical or related product can make it possible to avoid overlooking certain trade-offs between sustainability impacts. It can also make

it possible to avoid shifting the burden from one aspect of sustainability to another, or from the present to the future. Related requirements for policies, and for enabling relevant actors in the sustainable chemistry field, are addressed in Part IV. When chemicals are managed along entire product life cycles, attention needs to be paid to other factors which can have an impact on sustainability. These factors include materials extraction; energy and water use during chemical synthesis and product manufacturing; chemicals' occurrence and behaviour in waste streams; and the prospects of recycling chemicals for renewed use. Types of assessment frameworks that can be applied in chemical management are shown in Figure 7.1 (Fantke and Ernststoff 2018).

7.2 Assessing trade-offs between different impacts, locations and life cycle stages

As a complement to assessing and managing chemical risks in a regulatory or substitution context (discussed in previous chapters of Part III), there is a growing need for approaches and tools that allow the assessment of trade-

Figure 7.1 Conceptual relationships of the main chemical management tools (adapted from Fantke and Ernstoff 2018, p. 787)



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offs in the wider context of sustainability. An overview of such approaches is given in this chapter. They include assessing the direct human health and environmental risks of chemical exposures consistently with the full range of impacts – on humans and the environment while considering social aspects – which are related to the production and use of chemicals during their life cycle, from raw material extraction, via synthesis and manufacturing, to final use and end-of-life handling.

Such impacts include (but are not limited to) climate change impacts associated with greenhouse gas (GHG) emissions during oil refining; the formation of fine particulate matter and ozone from fuel combustion; the impacts on ecosystems of acidifying and eutrophying substances from agricultural emissions; energy use and emissions of harmful processing chemicals during chemical synthesis; and land and water use impacts of manufacturing and waste handling processes (Hauschild and Huijbregts 2015). The case for integrating the potential impacts of climate change as a consideration in assessments in general has

been addressed, for example, in the US EPA *Climate Change Adaptation Implementation Plan*, which acknowledges the need to integrate the impacts of climate change into assessments insofar as these impacts could affect chemical safety (US EPA 2014).

Accounting for impacts in a wider sustainability context is key to progress in meeting the Sustainable Development Goals. Often certain types of impacts cannot be reduced without introducing trade-offs with others (this type of trade-off is sometimes referred to as “burden-shifting”). An example of burden-shifting is the move from petroleum-derived to bio-based polymers, which in most cases reduces GHG emissions but also results in soil degradation, toxicity and eutrophication if pesticides and fertilizers are not applied correctly in bio-feedstock production (Hottle, Biilec and Landis 2013). Burden-shifting may also occur between chemical life cycle stages. An example is the reduction of sourcing of virgin raw materials through increased recycling, which can result in exposure to harmful residues in recyclates (Pivnenko and Astrup 2016). It is important to

look beyond impacts on, for example, workers, consumers or particular ecosystems and to assess all relevant impacts on humans and the environment during the entire chemical or product life cycle. At the same time, it is important to keep assessments practical – that is, focused on the most relevant impacts associated with the chemical-product combination being considered.

An adequate and sound assessment of chemicals-related sustainability will benefit from meeting the following criteria:

- › The assessment offers a consistent basis for comparing human health and environmental risks with other types of impacts.
- › It identifies relevant impact categories and sustainability metrics adapted to the application being considered, in order to limit effort and avoid being distracted by minor issues or negligible impacts.
- › It covers all product and chemical life cycle stages.
- › It is able to screen exposures and impacts of a large number of chemical-product combinations, considering chemical properties and product properties as well as people who will be exposed (e.g. workers, consumers and the general population).

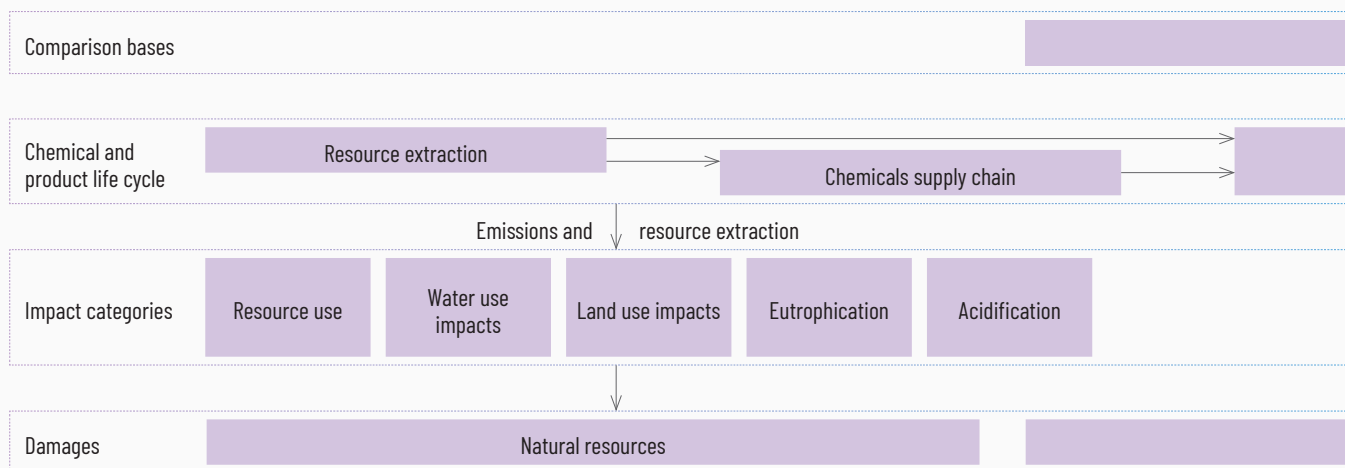
7.3 Sustainability assessment tools for chemicals

While certain sustainability assessment tools, such as carbon footprints and water footprints, adequately represent a company's environmental sustainability performance up to a point, these tools are restricted to particular areas of concern. They do not consider all relevant sustainability impacts in order to ensure overall minimized impacts on humans and the environment (Ridoutt *et al.* 2015). A change of perspective is therefore needed when looking at chemicals-related impacts.

To address the entire chemical or product life cycles in a wider sustainability context, several types of tools and methods exist that build on life cycle thinking. They range from political instruments, international agreements and international standards to procedural and analytical tools. Political instruments include regulations on supply chain and waste/end-of-life management or on integrated environmental management interventions. An example is the EU's Integrated Pollution Prevention and Control Directive 2010/75/EU (EC 2010).

International standards refer mainly to the International Organization for Standardization (ISO) 14000 family of environmental management standards (ISO 2018). Several of these standards are directly concerned with procedural and

Figure 7.2 General structure of the life cycle assessment (LCA) framework



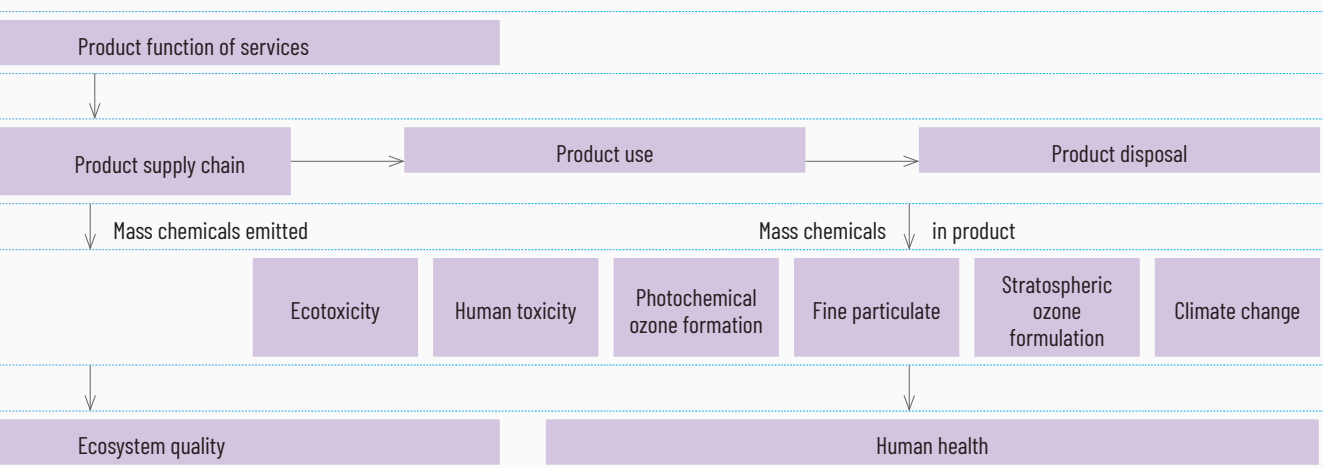


analytical life cycle management (LCM) tools. LCM encourages a holistic management perspective. It covers the entire chemical or product life cycle and calls for managerial decisions that consider health and environmental impacts. LCM provides an opportunity to promote long-term achievements in order to minimize the environmental and socio-economic burden while maximizing economic and social value (Bey 2018). Applying a life cycle perspective is even more relevant in regard to advancing a circular economy, closing material loops along entire chemical and product life cycles and creating self-sustaining production systems. More specific procedural tools include, among others, eco-

design (defined in ISO 14006), environmental labels and declarations (defined in the ISO 14020-14025 series) and environmental performance evaluation (defined in ISO 14030 and 14031). A method for assessing the economic, social and environmental sustainability performance of agricultural production at the farm level is the Response-Inducing Sustainability Evaluation (RISE) (Bern University of Applied Sciences 2017).

The most relevant analytical tool with a focus on the entire life cycle of chemicals and products is life cycle assessment (LCA), which is defined in the ISO 14040-14049 series (ISO 2018). The use of LCA to evaluate the environmental performance

(Fantke *et al.* 2019, submitted)



of products, services and technologies across sectors and countries has received increasing attention in the last two decades. Not only is LCA applied by individual companies. It is also being used as a method to evaluate 25 industry sectors in the context of the European pilot project series on the Product Environmental Footprint (PEF) and the Organization Environmental Footprint (OEF) (EC 2013).

LCA consists of four phases: goal and scope definition; life cycle inventory (LCI) analysis; life cycle impact assessment (LCIA); and interpretation. The LCI determines resources use, and chemical or pollutant emissions, based on a common product function. The LCIA phase focuses on characterizing the impacts of these LCI flows in several impact categories, such as global warming, human toxicity, ecotoxicity and water use (Figure 7.2). These impact categories cover three major areas of protection: human health; ecosystem quality; and natural resources (Verones *et al.* 2017). This allows not only assessing and comparing the different life cycle stages of a product or service, but also consistently assessing trade-offs between different impacts based on their relative damage (Hauschild 2005; Hellweg and Milà i Canals 2014).

7.4 Assessing chemicals' impacts in a life cycle-based comparative framework

When focusing on chemicals, it is important to assess their risks consistently with other types of impacts on human health and the environment. Several approaches, such as USEtox (Henderson *et al.* 2011; Rosenbaum *et al.* 2011), have been developed at the interface between risk assessment and LCA to adapt exposure and dose-response information for use within a comparative life cycle-based framework (Fantke *et al.* 2016).

Figure 7.3 shows the elements of such a comprehensive framework for evaluating chemicals and products in the global supply chain and their potential impacts on humans and the environment. Key elements include:

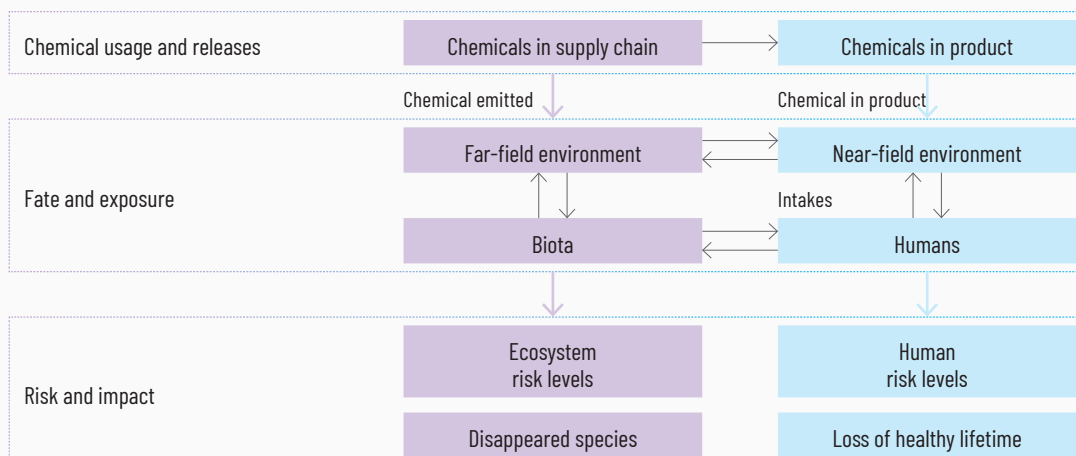
- › quantifying during the product life cycle – to the extent possible – the chemical use and the mass emitted to the far-field environment within the supply chain, or the chemical mass that enters a defined compartment of entry in the consumer's near-field environment;
- › capturing fate and exposure processes that result in transfers of chemicals between any near-field compartments (e.g. indoor air, the inside of objects) and far-field compartments (e.g. freshwater, ambient air) until finally reaching biota or humans;
- › combining human intake via all relevant exposure pathways with dose-response, severity or other hazard information to assess risk or impact levels; and
- › combining environmental concentrations with concentration-response information to assess related fractions of species that have disappeared or are affected due to chemical exposure in different environmental compartments (Verones *et al.* 2017).

In addition, for chemicals-based assessment not all impact categories are equally important. There is a need for a screening-level assessment of alternatives, which (where possible) is quantitative, life cycle-based, and able to serve both life cycle assessment (LCA) and chemical alternatives assessment (CAA). Such a life cycle-based alternatives assessment needs to quantify exposure and life cycle impacts consistently and efficiently over the main life cycle stages, avoiding “paralysis by analysis” in order to meet the time constraints of a screening assessment while ensuring scientific rigour (Fantke *et al.* 2019).

Strategic life cycle assessment: also considering socio-ecological sustainability

Tools such as The Natural Step's Strategic Life Cycle Assessment (SLCA) can be used to provide an overview of the full scope of sustainability at the product level. SLCA is an effective approach for assessment, capacity building and innovation within and beyond individual organizations (The Natural Step [TNS] 2018). It goes beyond inherent chemical or product properties and

Figure 7.3 Elements of a comprehensive framework to evaluate global chemical supply chain impacts on humans and the environment (based on Fantke *et al.* 2016, p. 510)



their potential exposures, which are commonly looked at, by connecting the product to science-based conditions for social and ecological sustainability (Ny *et al.* 2006). The principles and qualitative approach of SLCA encourage thinking strategically about the management of chemicals and waste in a broader context. They can stimulate innovation to prevent regrettable substitutions and burden-shifting in a circular economy (TNS 2018).

7.5 Potential measures to further advance approaches to sustainability assessment

Stakeholders may find value in the further development and use of wider sustainability assessment methods, including life cycle assessment tools, while acknowledging that informed choices have to be made about when

and how to use these methodologies. Taking into account the preceding analysis, stakeholders may wish to consider the following measures to further advance approaches to sustainability assessment:

- › During the chemical risk management decision-making process, consider the need to identify potential trade-offs in a wider sustainability context.
- › In considering the benefits of sustainability assessment methods, take into account regulatory priorities and resource considerations, while avoiding “paralysis by analysis” through focusing on the most relevant sustainability aspects.
- › Scale up the further development and use of life cycle assessment tools and life cycle management practices across sectors.

References

Chapter 1

American Chemical Society (2018). Definitions of hazard assessment. <https://www.acs.org/content/acs/en/about/governance/committees/chemicalsafety/hazard-assessment/tools/definitions.html>. Accessed 31 May 2018.

Berggren, E., Amcoff, P., Benigni, R., Blackburn, K., Carney, E., Cronin, M., Deluyker, H., Gautier, F., Judson, R.S., Kass, G.E.N., Keller, D., Knight, D., Lilienblum, W., Mahony, C., Rusyn, I., Schultz, T., Schwarz, M., Schüürmann, G., White, A., Burton, J., Lostia, A.M., Munn, S. and Worth, A. (2015). Chemical safety assessment using read-across: assessing the use of novel testing methods to strengthen the evidence base for decision making. *Environmental Health Perspectives* 123(12), 1232-1240. <https://doi.org/10.1289/ehp.1409342>.

Beronius, A., Hanberg, A., Zilliacus, J. and Rudén, C. (2014). Bridging the gap between academic research and regulatory health risk assessment of Endocrine Disrupting Chemicals. *Current Opinion in Pharmacology* 19, 99-104. <https://doi.org/10.1016/j.COPH.2014.08.005>.

Chemical Inspection and Regulation Service (2012a). Korea Toxic Chemicals Control Act (TCCA). http://www.cirs-reach.com/KoreaTCCA/Korea_Toxic_Chemicals_Control_Act_TCCA.html. Accessed 31 May 2018.

Chemical Inspection and Regulation Service (2012b). Turkish REACH-like chemical regulation. http://www.cirs-reach.com/Turkey/Turkey_Chemical_Regulation_Inventory_and_Control_of_Chemicals.html. Accessed 31 May 2018.

Chemical Inspection and Regulation Service (2017). MEP revised the data requirements under guidance documents for new chemical substance notification in China, 8 July. <http://www.cirs-reach.com/news-and-articles/MEP-Revised-the-Data-Requirements-under-Guidance-Documents-for-New-Chemical-Substance-Notification-in-China.html>. Accessed 30 December 2018.

ChemSafetyPro (2017). How to comply with Chemicals Control Act (CCA) in Korea. https://www.chemsafetypro.com/Topics/Korea/Introduction_to_Korean_Chemicals_Control_Act.html. Accessed 23 August 2018.

ChemSafetyPro (2018). How to Comply with Amended K-REACH Regulation 2018. https://www.chemsafetypro.com/Topics/Korea/Korea_REACH.html. Accessed 30 December 2018.

Colaïanna, M., Ilmjärv, S., Peterson, H., Kern, I., Julien, S., Baquió, M., Pallocca, G., Bosgra, S., Sachinidis, A., Hengstler, J.G., Leist, M. and Krause, K.-H. (2017). Fingerprinting of neurotoxic compounds using a mouse embryonic stem cell dual luminescence reporter assay. *Archives of Toxicology* 91(1), 365-391. <https://doi.org/10.1007/s00204-016-1690-2>.

Cynober, T. (2018). Could stem cells replace animal testing in drug development? 14 May. <https://labiotech.eu/animal-testing-stem-cells/>. Accessed 9 June 2018.

Delrue, N., Sachana, M., Sakuratani, Y., Gourmelon, A., Leinala, E. and Diderich, R. (2016). The adverse outcome pathway concept: a basis for developing regulatory decision-making tools. *Alternatives to Laboratory Animals* 44(5), 417-429. <http://www.ncbi.nlm.nih.gov/pubmed/27805824>.

Dimitrov, S.D., Diderich, R., Sobanski, T., Pavlov, T.S., Chankov, G. V., Chapkanov, A.S., Karakolev, Y.H., Temelkov, S.G., Vasilev, R.A., Gerova, K.D., Kuseva, C.D., Todorova, N.D., Mehmed, A.M., Rasenberg, M. and Mekenyan, O.G. (2016). QSAR Toolbox – workflow and major functionalities. *SAR and QSAR in Environmental Research* 27(3), 203-219. <https://doi.org/10.1080/1062936X.2015.1136680>.

Environment and Climate Change Canada (2016). *Chemicals Management Plan (CMP) Science Committee Objectives Paper: Meeting No. 5; 16-17 November 2016. Integrating New Approach Methodologies within the CMP: Identifying Priorities for Risk Assessment, Existing Substances Risk Assessment Program*. http://www.ec.gc.ca/ese-ees/172614CE-D9F6-43DA-A528-B8175438210F/Objectives%20Paper%20November%202016_EN.pdf.

European Chemical Industry Council Long-Range Research Initiative (2017). AMBIT. <http://cefic-lri.org/toolbox/ambit/>. Accessed 4 August 2018.

European Chemicals Agency (2016a). *Chemicals Presenting Priority Setting Challenges (2016) Presentation by M. Rasenberg at the OECD Working Party on Hazard Assessment*. Paris.

European Chemicals Agency (2016b). *ECHA's Ambition Towards 2025*. Helsinki. https://echa.europa.eu/documents/10162/2200151/mb_46_2016_echa_ambition_towards_2025_incl_annex_en.pdf/45c509e5-5ed3-bdb7-7515-3a6dbca9d727

European Chemicals Agency (2017a). Endpoint specific guidance. In *Guidance on information requirements and chemical safety assessment*. Chapter T. 7a. 1-610. <https://doi.org/10.2823/337352>.

European Chemicals Agency (2017b). *Non-Animal Approaches – Current Status of Regulatory Applicability Under the REACH, CLP and Biocidal Products Regulations*. https://echa.europa.eu/documents/10162/22931011/non_animal_approaches_en.pdf/87ebb68f-2038-f597-fc33-f4003e9e7d7d.

European Chemicals Agency (2017c) *Guidance on Information Requirements and Chemical Safety Assessment. Appendix R.6-1 for Nanomaterials Applicable to the Guidance on QSARs and Grouping of Chemicals. Version 1.0.* https://echa.europa.eu/documents/10162/23036412/appendix_r6_nanomaterials_en.pdf/71ad76f0-ab4c-fb04-acba-074cf045eaaa.

European Chemicals Agency (2017d). *The Use of Alternatives to Testing on Animals for the REACH Regulation*. https://echa.europa.eu/documents/10162/13639/alternatives_test_animals_2017_en.pdf.

European Chemicals Agency (2017e). Guest column: are REACH data appropriate for hazard identification and risk assessment? ECHA Newsletter No. 4, November. <https://newsletter.echa.europa.eu/home/-/newsletter/entry/guest-column-are-reach-data-appropriate-for-hazard-identification-and-risk-assessment->. Accessed 1 January 2019.

European Chemicals Agency (2018). New database on Candidate List substances in articles by 2021, 11 July. <https://echa.europa.eu/nl/-/new-database-on-candidate-list-substances-in-articles-by-2021>. Accessed 30 December 2018.

European Chemicals Agency (n.d. a). REACH legislation. <https://echa.europa.eu/regulations/reach/legislation>. Accessed 4 August 2018.

European Chemicals Agency (n.d. b). Search for chemicals. <https://echa.europa.eu/information-on-chemicals>. Accessed 30 December 2018.

European Chemicals Agency (n.d. c). Chesar: Chemical safety assessment and reporting tool. <https://chesar.echa.europa.eu/>. Accessed 24 August 2018.

European Chemicals Agency and Organisation for Economic Co-operation and Development (2018). IUCLID 6. <https://iuclid6.echa.europa.eu/>. Accessed 1 August 2018.

European Chemicals Agency and United States Environmental Protection Agency (2016). *ECHA-EPA Workshop: Accelerating the Pace for (Chemical) Risk Assessment (APCRA)*. https://ntp.niehs.nih.gov/ntp/about_ntp/bsc/2017/december/meetingmaterials/bucher_echa_508.pdf.

European Commission (2006). Regulation (EC) No. 1907/2006 of the European parliament and of the council of 18 December 2006 concerning the registration, evaluation, authorisation and restriction of chemicals (REACH), establishing a European chemicals agency, amending directive 1999. *Official Journal of the European Union* L 396, 3-280. <https://doi.org/10.04.2014>.

European Commission (2018). Nanomaterials in REACH and CLP. http://ec.europa.eu/environment/chemicals/nanotech/reach-clp/index_en.htm. Accessed 1 January 2019.

Gottardo, S., Alessandrelli, M., Amenta, V., Atluri, R., Barberio, G., Bekker, C., Bergonzo, P., Bleeker, E., Booth, A.M., Borges, T., Buttol, P., Carlander, D., Castelli, S., Chevillard, S., Clavaguera, S., Dekkers, S., Delpivo, C., Di Prospero Fanghella, P., Dusinska, M., Einola, J., Ekokoski, E., Fito, C., Gouveia, H., Grall, R., Hoehener, K., Johanson, G., Laux, P., Lehmann, Hans Christian, Leinonen, R., Mech, A., Micheletti, Christian, Noorlander, C., Olof-Mattsson, M., Oomen, A., Quiros Pseudo, L., Polci, M.L. and Prina-Mello, Adriele., Rasmussen, K., Rauscher, H., Sanchez Jimenez, A., Riego Sintes, J., Scalbi, S., Sergent, J.-A., Stockmann-Juvala, H., Simko, M., Sips, A., Suarez, B., Sumrein, A., van Tongeren, M., Vazquez, S., Vital, N., Walsler, T., Wijnhoven, S. and Crutzen, H. (2017). *NANoREG Framework for the Safety Assessment of Nanomaterials*. Gottardo, S., Crutzen, H. and Jantunen, P. (eds.). Ispra: Publications Office of the European Union. <https://doi.org/10.2760/245972>.

Government of Canada (2016a). Chemicals management plan, 2 June. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan.html>. Accessed 1 January 2019.

Government of Canada (2016b). Substance groupings initiative, 8 October. <https://www.canada.ca/en/health-canada/services/chemical-substances/substance-groupings-initiative.html>. Accessed 1 January 2019.

Government of Canada (2017). Chemicals management plan science committee: Mid-term progress report February 2014 – June 2015, 13 October. <https://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=8823FEF0-1#toc7b>. Accessed 1 January 2019.

He, N. (2019). South Korea issues 364 CMR substances for reporting by 2021, 1 January. *Chemlinked*. <https://chemlinked.com/news/chemical-news/south-korea-issues-364-cmr-substances-registration-2021>. Accessed 3 January 2019.

International Labour Organization (2018). International chemical safety cards. http://www.ilo.org/safework/info/publications/WCMS_113134/lang-en/index.htm. Accessed 1 January 2019.

- Japan Ministry of Economy, Trade and Industry (2016). What is CSCL (Chemical Substances Control Law), 4 March. http://www.meti.go.jp/policy/chemical_management/english/cscl/about.html. Accessed 1 January 2019.
- Jeliazkova, N., Koch, V., Li, Q., Jensch, U., Reigl, J.S., Kreiling, R., Georgiev, I. and Hubesch, B. (2016). Linking LRI AMBIT chemoinformatic system with the IUCLID substance database to support read-across of substance endpoint data and category formation. *Toxicology Letters* 258, 114-115. <https://doi.org/10.1016/j.toxlet.2016.06.1469>.
- Krewski, D., Acosta, D., Andersen, M., Anderson, H., Bailar, J.C., Boekelheide, K., Brent, R., Charnley, G., Cheung, V.G., Green, S., Kelsey, K.T., Kerkvliet, N.I., Li, A.A., McCray, L., Meyer, O., Patterson, R.D., Pennie, W., Scala, R.A., Solomon, G.M., Stephens, M., Yager, J. and Zeise, L. (2010). Toxicity testing in the 21st century: a vision and a strategy. *Journal of Toxicology and Environmental Health. Part B, Critical Reviews* 13, 51-138. <https://doi.org/10.1080/10937404.2010.483176>.
- Lexology (2018). What's new with China's chemical import and export regulatory programs, 21 February. <https://www.lexology.com/library/detail.aspx?g=a1ebde22-4b14-4d09-8ca3-c9878028a444>. Accessed 1 January 2019.
- Maertens, A., Anastas, N., Spencer, P.J., Stephens, M., Goldberg, A. and Hartung, T. (2014). Green toxicology. *Alternatives to Animal Experimentation* 31(3), 243-249. <http://www.ncbi.nlm.nih.gov/pubmed/25061898>.
- Organisation for Economic Co-operation and Development (2003). *Descriptions of Selected Key Generic Terms Used in Chemical Hazard/Risk Assessment*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO\(2003\)15&docLanguage=En](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2003)15&docLanguage=En).
- Organisation for Economic Co-operation and Development (2005). *Guidance Document on the Validation and International Acceptance of New or Updated Test Methods for Hazard Assessment*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?doclanguage=en&cote=env/jm/mono\(2005\)14](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?doclanguage=en&cote=env/jm/mono(2005)14).
- Organisation for Economic Co-operation and Development (2007). *Guidance Document on the Validation of (Quantitative) Structure-Activity Relationships*. <http://www.oecd.org/fr/securitechimique/risques/38130292.pdf>.
- Organisation for Economic Co-operation and Development (2010). *Cutting Costs in Chemicals Management: How OECD Helps Governments and Industry*. <https://doi.org/10.1787/9789264085930-en>.
- Organisation for Economic Co-operation and Development (2014a). *Guidance on Grouping of Chemicals*. 2nd edn. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2014\)4&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2014)4&doclanguage=en).
- Organisation for Economic Co-operation and Development (2014b). *New Guidance Document on an Integrated Approach on Testing and Assessment (IATA) for Skin Corrosion and Irritation*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2014\)19&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2014)19&doclanguage=en).
- Organisation for Economic Co-operation and Development (2016). *Report on the Pilot Project on Assessing the Potential Development of a Global List of Classified Chemicals*. [https://one.oecd.org/document/ENV/JM/MONO\(2016\)43/en/pdf](https://one.oecd.org/document/ENV/JM/MONO(2016)43/en/pdf).
- Organisation for Economic Co-operation and Development (2017). *Guidance Document for the Use of Adverse Outcome Pathways in Developing Integrated Approaches to Testing and Assessment (IATA)*. https://issuu.com/oecd.publishing/docs/guidance_document_for_the_use_of_ad.
- Organisation for Economic Co-operation and Development (2018a). Safety of manufactured nanomaterials. <http://www.oecd.org/science/nanosafety/>. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018b). OECD guidelines for the testing of chemicals, section 1: physical-chemical properties. https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-1-physical-chemical-properties_20745753. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018c). OECD guidelines for the testing of chemicals, section 2: effects on biotic systems. https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-2-effects-on-biotic-systems_20745761. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018d). *OECD guidelines for the testing of chemicals, section 3: environmental fate and behaviour*. https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-3-degradation-and-accumulation_2074577x. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018e). OECD guidelines for the testing of chemicals, section 4: health effects. https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018f). Good laboratory practice (GLP). <http://www.oecd.org/chemicalsafety/testing/good-laboratory-practiceglp.htm>. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018g). OECD test guidelines for the chemicals. <http://www.oecd.org/chemicalsafety/testing/oecdguidelinesforthetestingofchemicals.htm>. Accessed 1 January 2019.

- Organisation for Economic Co-operation and Development (2018h). Mutual acceptance of data (MAD). <http://www.oecd.org/chemicalsafety/testing/mutualacceptanceofdatamad.htm>. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018i). Animal welfare: OECD considers animal welfare in the development of test guidelines. <http://www.oecd.org/chemicalsafety/testing/animal-welfare.htm>. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018j). The OECD QSAR toolbox. <http://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm>. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (n.d.). The global portal to information on chemical substances. *eChemPortal*. <https://www.echemportal.org/echemportal/index.action>. Accessed 1 January 2019
- Parliament of the Commonwealth of Australia (2017). Industrial Chemicals Bill 2017. https://www.aph.gov.au/Parliamentary_Business/Bills_Legislation/Bills_Search_Results/Result?bld=r5885. Accessed 1 January 2019.
- Persson, L., Karlsson-Vinkhuyzen, S., Lai, A., Persson, Å. and Fick, S. (2017). The globally harmonized system of classification and labelling of chemicals: explaining the legal implementation gap. *Sustainability* 9(12), 1-21. <https://doi.org/10.3390/su9122176>.
- SGS (2017). Turkey publishes EU REACH-like regulation, 7 July. <https://www.sgs.com/en/news/2017/07/safeguards-10217-turkey-publishes-eu-reach-like-regulation>. Accessed 1 January 2019
- Swedish Chemicals Agency (2018). PRIO – a tool for risk reduction of chemicals. Hazard assessment. <https://www.kemi.se/en/prio-start/chemicals-in-practical-use/hazard-assessment>. Accessed 1 January 2019.
- United Nations (2017). *Globally Harmonised System for Classification and Labelling of Chemicals (GHS)*. 7th revised edn. New York and Geneva. ST/SG/AC.10/30/Rev.7. https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev07/English/ST_SG_AC10_30_Rev7e.pdf. Accessed 31 May 2018.
- United Nations Economic Commission for Europe (n.d.). GHS implementation. https://www.unece.org/trans/danger/publi/ghs/implementation_e.html. Accessed 1 January 2019.
- United States Environmental Protection Agency (2010). *TSCA New Chemicals Program (NCP) Chemical Categories*. https://www.epa.gov/sites/production/files/2014-10/documents/ncp_chemical_categories_august_2010_version_0.pdf.
- United States Environmental Protection Agency (2016). Research on nanomaterials, 18 October. <https://www.epa.gov/chemical-research/research-nanomaterials>. Accessed 1 January 2019.
- United States Environmental Protection Agency (2017). Endocrine Disruptor Screening Program (EDSP) Overview, 22 February. <https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-overview>. Accessed 1 January 2019.
- United States Environmental Protection Agency (2018a). Legislative and regulatory authority for reviewing new chemicals under TSCA, 15 November. <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/legislative-and-regulatory-authority>. Accessed 1 January 2019.
- United States Environmental Protection Agency (2018b). The Frank R. Lautenberg Chemical Safety for the 21st Century Act. <https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/frank-r-lautenberg-chemical-safety-21st-century-act>. Accessed 1 January 2019.
- United States Environmental Protection Agency (2018c). Exploring ToxCast data: downloadable data. <https://www.epa.gov/chemical-research/toxicity-forecaster-toxcasttm-data>. Accessed 1 January 2019.
- United States Environmental Protection Agency (2018d). *Strategic Plan to Promote the Development and Implementation of Alternative Test Methods Within the TSCA Program*. https://www.epa.gov/sites/production/files/2018-06/documents/epa_alt_strat_plan_6-20-18_clean_final.pdf.
- United States Environmental Protection Agency (2018e). Alternative test methods and strategies to reduce vertebrate animal testing. <https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/alternative-test-methods-and-strategies-reduce>. Accessed 1 January 2019.
- United States Interagency Coordinating Committee on the Validation of Alternative Methods (2018). *A Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medical Products in the United States*. <https://dx.doi.org/10.22427/NTP-ICCVAM-ROADMAP2018>.
- United States National Academy of Sciences (2007). *Toxicity Testing in the 21st Century: A Vision and a Strategy*. <https://www.nap.edu/catalog/11970/toxicity-testing-in-the-21st-century-a-vision-and-a>.
- United States National Library of Medicine (2018). Hazard identification. *ToxTutor*. <https://tox.tutor.nlm.nih.gov/06-002.html>. Accessed 1 January 2019.
- Vinken, M., Knapen, D., Vergauwen, L., Hengstler, J.G., Angrish, M. and Whelan, M. (2017). Adverse outcome pathways: a concise introduction for toxicologists. *Archives of Toxicology* 91(11), 3697-3707. <https://doi.org/10.1007/s00204-017-2020-z>.

Wexler, P., Judson, R., de Marcellus, S., de Knecht, J. and Leinala, E. (2016). Health effects of toxicants: online knowledge support. *Life Sciences* 145, 284-293. <https://doi.org/10.1016/j.lfs.2015.10.002>.

World Health Organization (2019). International programme on chemical safety: international chemical safety cards. <http://www.who.int/ipcs/publications/icsc/en/>. Accessed 3 January 2019.

Chapter 2

Altenburger, R., Backhaus, T., Boedeker, W., Faust, M. and Scholze, M. (2013). Simplifying complexity: mixture toxicity assessment in the last 20 years. *Environmental Toxicology and Chemistry* 32(8), 1685-1687. <https://doi.org/10.1002/etc.2294>.

Aylward, L.L., Green, E., Porta, M., Toms, L.-M., Den Hond, E., Schulz, C., Gasull, M., Pumarega, J., Conrad, A., Kolossa-Gehring, M., Schoeters, G. and Mueller, J.F. (2014). Population variation in biomonitoring data for persistent organic pollutants (POPs): an examination of multiple population-based datasets for application to Australian pooled biomonitoring data. *Environment International* 68, 127-138. <https://doi.org/10.1016/j.envint.2014.03.026>.

Becker, K., Seiwert, M., Casteleyn, L., Joas, R., Joas, A., Biot, P., Aerts, D., Castaño, A., Esteban, M., Angerer, J., Koch, H.M., Schoeters, G., Hond, E., Sepai, O., Exley, K., Knudsen, L.E., Horvat, M., Bloemen, L. and Kolossa-Gehring, M. (2014). A systematic approach for designing a HBM pilot study for Europe. *International Journal of Hygiene and Environmental Health* 217(2-3), 312-322. <https://doi.org/10.1016/j.ijheh.2013.07.004>.

Cohen Hubal, E.A., Richard, A., Aylward, L., Edwards, S., Gallagher, J., Goldsmith, M.-R., Isukapalli, S., Tornero-Velez, R., Weber, E. and Kavlock, R. (2010). Advancing exposure characterization for chemical evaluation and risk assessment. *Journal of Toxicology and Environmental Health, Part B* 13(2-4), 299-313. <https://doi.org/10.1080/10937404.2010.483947>.

Consortium to Perform Human Biomonitoring on a European Scale (2016). Human biomonitoring. <http://www.eu-hbm.info/cophes/human-biomonitoring>. Accessed 2 January 2019.

Csiszar, S.A., Ernstoff, A.S., Fantke, P. and Jolliet, O. (2017). Stochastic modeling of near-field exposure to parabens in personal care products. *Journal of Exposure Science and Environmental Epidemiology* 27(2), 152-159. <http://doi.org/10.1038/jes.2015.85>.

Csiszar, S.A., Ernstoff, A.S., Fantke, P., Meyer, D.E. and Jolliet, O. (2016). High-throughput exposure modeling to support prioritization of chemicals in personal care products. *Chemosphere* 163, 490-498. <https://doi.org/10.1016/j.chemosphere.2016.07.065>.

Di Guardo, A., Gouin, T., MacLeod, M. and Scheringer, M. (2018). Environmental fate and exposure models: advances and challenges in 21st century chemical risk assessment. *Environmental Science: Processes & Impacts* 20(1), 58-71. <https://doi.org/10.1039/C7EM00568G>.

Escher, B.I., Hackermüller, J., Polte, T., Scholz, S., Aigner, A., Altenburger, R., Böhme, A., Bopp, S.K., Brack, W., Busch, W., Chadeau-Hyam, M., Covaci, A., Eisenräger, A., Galligan, J.J., Garcia-Reyero, N., Hartung, T., Hein, M., Herberth, G., Jahnke, A., Kleinjans, J., Klüver, N., Krauss, M., Lamoree, M., Lehmann, I., Luckenbach, T., Miller, G.W., Müller, A., Phillips, D.H., Reemtsma, T., Rolle-Kampczyk, U., Schüürmann, G., Schwikowski, B., Tan, Y.-M., Trump, S., Walter-Rohde, S. and Wambaugh, J.F. (2017). From the exposome to mechanistic understanding of chemical-induced adverse effects. *Environment International* 99, 97-106. <https://doi.org/10.1016/j.envint.2016.11.029>.

European Chemicals Agency (2016). Environmental exposure assessment. In *Guidance on Information Requirements and Chemical Safety Assessment*. Chapter R.16. 1-178. https://echa.europa.eu/documents/10162/13632/information_requirements_r16_en.pdf.

European Chemicals Agency (2018a). Chesar: chemical safety assessment and reporting tool. <https://chesar.echa.europa.eu/>. Accessed 30 December 2018.

European Chemicals Agency (2018b). Workshop on EUSES update needs. <https://echa.europa.eu/nl/-/workshop-on-euses-update-needs>. Accessed 30 December 2018.

European Commission (2018) Information platform for chemical monitoring: enhancing access to chemical data, 10 March. <https://ipchem.jrc.ec.europa.eu/RDSIdiscovery/ipchem/index.html>. Accessed 30 December 2018.

Fantke, P., Ernstoff, A.S., Huang, L., Csiszar, S.A. and Jolliet, O. (2016). Coupled near-field and far-field exposure assessment framework for chemicals in consumer products. *Environment International* 94, 508-518. <https://doi.org/10.1016/j.envint.2016.06.010>.

Faustman, E.M. and Omenn, G.S. (2013). Risk assessment. In *Casarett and Doull's Toxicology: The Basic Science of Poisons*. 8th edn. Klaassen, C.D. (ed.). McGraw-Hill Education. Chapter 4. 123-149. <https://accesspharmacy.mhmedical.com/content.aspx?sectionid=53483723&bookid=958>.

Gligorovski, S. and Abbatt, J.P.D. (2018). An indoor chemical cocktail. *Science* 359(6376), 632-633. <https://doi.org/10.1126/science.aar6837>.

- Goldsmith, M.-R., Grulke, C.M., Brooks, R.D., Transue, T.R., Tan, Y.M., Frame, A., Egeghy, P.P., Edwards, R., Chang, D.T., Tornero-Velez, R., Isaacs, K., Wang, A., Johnson, J., Holm, K., Reich, M., Mitchell, J., Vallero, D.A., Phillips, L., Phillips, M., Wambaugh, J.F., Judson, R.S., Buckley, T.J. and Dary, C.C. (2014). Development of a consumer product ingredient database for chemical exposure screening and prioritization. *Food and Chemical Toxicology* 65, 269-279. <https://doi.org/10.1016/J.FCT.2013.12.029>.
- Government of Canada (2018). Canadian health measures survey, 23 August. <https://www.statcan.gc.ca/eng/survey/household/5071>. Accessed 24 August 2018.
- Heffernan, A.L., Aylward, L.L., Toms, L.-M.L., Sly, P.D., Macleod, M. and Mueller, J.F. (2014). Pooled biological specimens for human biomonitoring of environmental chemicals: opportunities and limitations. *Journal of Exposure Science & Environmental Epidemiology* 24(3), 225-232. <https://doi.org/10.1038/jes.2013.76>.
- Heffernan, A.L., Baduel, C., Toms, L.M.L., Calafat, A.M., Ye, X., Hobson, P., Broomhall, S. and Mueller, J.F. (2015). Use of pooled samples to assess human exposure to parabens, benzophenone-3 and triclosan in Queensland, Australia. *Environment International* 85, 77-83. <https://doi.org/10.1016/J.ENVINT.2015.09.001>.
- Human and Environmental Risk Assessment (n.d.). HERA Initiative. <https://www.heraproject.com/Initiative.cfm>. Accessed 30 December 2018.
- Human Biomonitoring for Europe (2018). About HBM4EU. <https://www.hbm4eu.eu/about-hbm4eu/>. Accessed 30 December 2018.
- International Labour Organization (1993). *Safety in the Use of Chemicals at work: An ILO Code of Practice*. https://www.ilo.org/wcmsp5/groups/public/---ed_protect/---protrav/---safework/documents/normativeinstrument/wcms_107823.pdf.
- International Labour Organization (2004). Monitoring in the workplace, 30 November. <https://www.ilo.org/legacy/english/protection/safework/cis/products/safetytm/chemcode/12.htm>. Accessed 24 August 2018.
- International Labour Organization (2011). Chemical exposure limits, 16 February. https://www.ilo.org/safework/info/publications/WCMS_151534/lang--en/index.htm. Accessed 24 August 2018.
- Isaacs, K.K., Glen, W.G., Egeghy, P., Goldsmith, M.-R., Smith, L., Vallero, D., Brooks, R., Grulke, C.M. and Özkaynak, H. (2014). SHEDS-HT: an integrated probabilistic exposure model for prioritizing exposures to chemicals with near-field and dietary sources. *Environmental Science & Technology* 48(21), 12750-12759. <https://doi.org/10.1021/es502513w>.
- Isaacs, K.K., Goldsmith, M.-R., Egeghy, P., Phillips, K., Brooks, R., Hong, T. and Wambaugh, J.F. (2016). Characterization and prediction of chemical functions and weight fractions in consumer products. *Toxicology Reports* 3, 723-732. <https://doi.org/10.1016/J.TOXREP.2016.08.011>.
- Kijko, G., Jolliet, O. and Margni, M. (2016). Occupational health impacts due to exposure to organic chemicals over an entire product life cycle. *Environmental Science & Technology* 50(23), 13105-13114. <https://doi.org/10.1021/acs.est.6b04434>.
- Kijko, G., Margni, M., Partovi-Nia, V., Doudrich, G. and Jolliet, O. (2015). Impact of occupational exposure to organic chemicals in life cycle assessment: a new framework based on measured concentrations and labor hours. *Environmental Science & Technology* 49(14), 8741-8750. <https://doi.org/10.1021/acs.est.5b00078>.
- Meesters, J.A., Koelmans, A.A., Quik, J.T., Hendriks, A.J. and van de Meent, D. (2014). Multimedia modeling of engineered nanoparticles with SimpleBox4nano: model definition and evaluation. *Environmental Science & Technology* 48(10). <https://www.ncbi.nlm.nih.gov/pubmed/24766433>.
- Netherlands National Institute for Public Health and the Environment (2018). ConsExpo, 20 November. <https://www.rivm.nl/en/Topics/C/ConsExpo>. Accessed 30 December 2018.
- Nordic Council of Ministers (2006). *Scoping Study on Releases from Products with a Proposal of the Next Steps*. <https://dx.doi.org/10.6027/tn2006-597>.
- Organisation for Economic Co-operation and Development (2008). *Complementing Guideline for Writing Emission Scenario Documents: The Life-cycle Step "Service-Life"*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2008\)41/rev1&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2008)41/rev1&doclanguage=en).
- Organisation for Economic Co-operation and Development (2012). *Description of Existing Models and Tools Used for Exposure Assessment: Results of OECD Survey*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO\(2012\)37&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2012)37&doclanguage=en).
- Organisation for Economic Co-operation and Development (2013). *Guidance Document for Exposure Assessment Based on Environmental Monitoring*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2013\)7&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2013)7&doclanguage=en).
- Organisation for Economic Co-operation and Development (2017). *Resource Compendium of PRTR Release Estimation Techniques, Part 4: Summary of Techniques for Releases from Products*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2017\)2/ann&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2017)2/ann&doclanguage=en).

- Organisation for Economic Co-operation and Development (2018a). Publications in the series on pollutant release and transfer registers. <http://www.oecd.org/chemicalsafety/pollutant-release-transfer-register/publicationsintheseriesonpollutantreleaseandtransferregisters.htm>. Accessed 31 May 2018.
- Organisation for Economic Co-operation and Development (2018b). Introduction to emission scenario documents. <http://www.oecd.org/env/ehs/risk-assessment/introductiontoemissionscenariodocuments.htm>. Accessed 31 May 2018.
- Organisation for Economic Co-operation and Development (2018c). OECD Pov and LRTP screening tool. <http://www.oecd.org/env/ehs/risk-assessment/oecdповandlrtpscreeningtool.htm>. Accessed 31 May 2018.
- Overcash, M. (2016). Environmental genome of industrial products (EGIP): the missing link for human health. *Green Chemistry* 18(12), 3600-3606. <https://doi.org/10.1039/C6GC00182C>.
- Pharos (2018). Pharos Project. <https://www.pharosproject.net/>. Accessed 5 June 2018.
- Posthuma, L., Dyer, S.D., de Zwart, D., Kapo, K., Holmes, C.M. and Burton, G.A. (2016). Eco-epidemiology of aquatic ecosystems: separating chemicals from multiple stressors. *Science of The Total Environment* 573, 1303-1319. <https://doi.org/10.1016/j.scitotenv.2016.06.242>.
- Ring, C.L., Arnot, J., Bennett, D.H., Egeghy, P.P., Fantke, P., Huang, L., Isaacs, K.K., Jolliet, O., Phillips, K.A., Price, P.S., Shin, H.M., Westgate, J.N., W, S.R. and F, W.J. (2018). Chemical exposure pathway prediction for screening and priority-setting. *Submitted to Environmental Science & Technology*.
- Rosenbaum, R.K., Bachmann, T.M., Gold, L.S., Huijbregts, M.A.J., Jolliet, O., Juraske, R., Koehler, A., Larsen, H.F., MacLeod, M., Margni, M., McKone, T.E., Payet, J., Schuhmacher, M., van de Meent, D. and Hauschild, M.Z. (2008). USEtox – the UNEP-SETAC toxicity model: recommended characterisation factors for human toxicity and freshwater ecotoxicity in life cycle impact assessment. *The International Journal of Life Cycle Assessment* 13(7), 532-546. <https://doi.org/10.1007/s11367-008-0038-4>.
- Rosenbaum, R.K., Huijbregts, M.A.J., Henderson, A.D., Margni, M., McKone, T.E., van de Meent, D., Hauschild, M.Z., Shaked, S., Li, D.S., Gold, L.S. and Jolliet, O. (2011). USEtox human exposure and toxicity factors for comparative assessment of toxic emissions in life cycle analysis: sensitivity to key chemical properties. *The International Journal of Life Cycle Assessment* 16(8), 710-727. <https://doi.org/10.1007/s11367-011-0316-4>.
- Scanlon, K.A., Lloyd, S.M., Gray, G.M., Francis, R.A. and LaPuma, P. (2015). An approach to integrating occupational safety and health into life cycle assessment: development and application of work environment characterization factors. *Journal of Industrial Ecology* 19(1), 27-37. <https://doi.org/10.1111/jiec.12146>.
- Secretariat of the Convention on Biological Diversity (2010). *Global Biodiversity Outlook 3*. <https://www.cbd.int/doc/publications/gbo/gbo3-final-en.pdf>.
- Shin, H.-M., Ernstoff, A., Arnot, J.A., Wetmore, B.A., Csiszar, S.A., Fantke, P., Zhang, X., McKone, T.E., Jolliet, O. and Bennett, D.H. (2015). Risk-based high-throughput chemical screening and prioritization using exposure models and in vitro bioactivity assays. *Environmental Science & Technology* 49(11), 6760-6771. <https://doi.org/10.1021/acs.est.5b00498>.
- United Nations Economic Commission for Europe (2018). Introduction: Kyiv Protocol on Pollutant Release and Transfer Registers. <https://www.unece.org/env/pp/prtr.html>. Accessed 30 December 2018.
- United Nations Environment Programme (2017). *Towards a Pollution-free Planet: Background Report*. https://wedocs.unep.org/bitstream/handle/20.500.11822/21800/UNEA_towardspollution_long%20version_Web.pdf?sequence=1&isAllowed=y.
- United Nations Environment Programme and World Health Organization (2013) *Results of the Global Survey on Concentrations in Human Milk of Persistent Organic Pollutants by the United Nations Environment Programme and the World Health Organization*. Geneva: Secretariat of the Stockholm Convention. http://wedocs.unep.org/bitstream/handle/20.500.11822/19392/UNEPPOPSCOP6INF33English_%281%29.pdf?sequence=1&isAllowed=y.
- United Nations Institute for Training and Research (2018). UNITAR PRTR Platform. <http://prtr.unitar.org/site/resources>. Accessed 31 May 2018.
- United States Centers for Disease Control and Prevention (2018a). National health and nutrition examination survey. <https://www.cdc.gov/nchs/nhanes/index.htm>. Accessed 1 June 2018.
- United States Centers for Disease Control and Prevention (2018b). National Report on Human Exposure to Environmental Chemicals, March. <https://www.cdc.gov/exposurereport/index.html>. Accessed 17 August 2018.
- United States Environmental Protection Agency (2016) ChemSTEER-chemical screening tool for exposures and environmental releases, 7 September. <https://www.epa.gov/tsca-screening-tools/chemsteer-chemical-screening-tool-exposures-and-environmental-releases>. Accessed 30 December 2018.

United States Environmental Protection Agency (2017a). Assessing human health risk from pesticides, 31 August. <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/assessing-human-health-risk-pesticides>. Accessed 3 June 2018.

United States Environmental Protection Agency (2017b). Predictive models and tools for assessing chemicals under the Toxic Substances Control Act (TSCA), 18 December. <https://www.epa.gov/tsca-screening-tools>. Accessed 30 December 2018.

United States Environmental Protection Agency (2017c). Environmental measurements and modeling: collection of methods, 3 October. <https://www.epa.gov/measurements-modeling/collection-methods>. Accessed 1 June 2018.

United States Environmental Protection Agency (2017d). Exposure assessment tools by tiers and types: aggregate and cumulative, 29 November. <https://www.epa.gov/expobox/exposure-assessment-tools-tiers-and-types-aggregate-and-cumulative>. Accessed 3 June 2018.

United States Environmental Protection Agency (2017e). Exposure assessment tools by chemical classes, 1 December. <https://www.epa.gov/expobox/exposure-assessment-tools-chemical-classes>. Accessed 1 June 2018.

United States Environmental Protection Agency (2018). Rapid chemical exposure and dose research, 9 October. <https://www.epa.gov/chemical-research/rapid-chemical-exposure-and-dose-research>. Accessed 30 December 2018.

van de Meent, D. and de Bruijn, J.H.M. (2007). Environmental exposure assessment. In *Risk assessment of chemicals: An introduction*. 2nd edn. van Leeuwen, C.J. and Vermeire, T. (eds). Dordrecht: Springer. Chapter 4. 159-194. <https://www.springer.com/gp/book/9781402061011>.

Wambaugh, J.F., Setzer, R.W., Reif, D.M., Gangwal, S., Mitchell-Blackwood, J., Arnot, J.A., Joliet, O., Frame, A., Rabinowitz, J., Knudsen, T.B., Judson, R.S., Egeghy, P., Vallero, D. and Cohen Hubal, E.A. (2013). High-throughput models for exposure-based chemical prioritization in the ExpoCast project. *Environmental Science & Technology* 47(15), 8479-8488. <https://doi.org/10.1021/es400482g>.

Wannaz, C., Franco, A., Kilgallon, J., Hodges, J. and Joliet, O. (2018). A global framework to model spatial ecosystems exposure to home and personal care chemicals in Asia. *Science of The Total Environment* 622-623, 410-420. <https://doi.org/10.1016/j.scitotenv.2017.11.315>.

World Health Organization (2004). *IPCS Harmonization Project – IPCS Risk Assessment Terminology*. <http://www.inchem.org/documents/harmproj/harmproj/harmproj1.pdf>.

Chapter 3

Ågerstrand, M. and Beronius, A. (2016). Weight of evidence evaluation and systematic review in EU chemical risk assessment: foundation is laid but guidance is needed. *Environment International* 92-93, 590-596. <https://doi.org/10.1016/j.envint.2015.10.008>.

American Chemistry Council (2018). Another milestone for the successful implementation of TSCA, 17 August. <https://blog.americanchemistry.com/2018/08/another-milestone-for-the-successful-implementation-of-tsca/>. Accessed 4 January 2019.

Backhaus, T. (2015). *An Additional Assessment Factor (MAF) – A Suitable Approach for Improving the Regulatory Risk Assessment of Chemical Mixtures?* Stockholm: Swedish Chemicals Agency. <https://www.kemi.se/global/rapporter/2015/rapport-5-15.pdf>.

Backhaus, T., Scheringer, M. and Wang, Z. (2018). Developing SAICM into a framework for the international governance of chemicals throughout their lifecycle: Looking beyond 2020. In *Integrated Environmental Assessment and Management*. Wiley-VCH Verlag GmbH & Co. KGaA. <https://doi.org/10.1002/3527607463>.

Brown, A.R., Whale, G., Jackson, M., Marshall, S., Hamer, M., Solga, A., Kabouw, P., Galay-Burgos, M., Woods, R., Nadzialek, S. and Maltby, L. (2017). Toward the definition of specific protection goals for the environmental risk assessment of chemicals: a perspective on environmental regulation in Europe. *Integrated Environmental Assessment and Management* 13(1), 17-37. <https://doi.org/10.1002/ieam.1797>.

Carusi, A., Davies, M.R., De Grandis, G., Escher, B.I., Hodges, G., Leung, K.M.Y., Whelan, M., Willett, C. and Ankley, G.T. (2018). Harvesting the promise of AOPs: an assessment and recommendations. *Science of The Total Environment* 628-629, 1542-1556. <https://doi.org/10.1016/j.scitotenv.2018.02.015>.

Chiu, W.A. (2017). *Chemical Risk Assessment and Translation to Socio-economic Assessments*. Paris: Organisation for Economic Co-operation and Development. <http://dx.doi.org/10.1787/a930054b-en>.

Environment and Climate Change Canada (2016). *Chemicals Management Plan (CMP) Science Committee Objectives Paper: Meeting No. 5; 16-17 November 2016. Integrating New Approach Methodologies within the CMP: Identifying Priorities for Risk Assessment, Existing Substances Risk Assessment Program*. http://www.ec.gc.ca/ese-ees/172614CE-D9F6-43DA-A528-B8175438210F/Objectives%20Paper%20November%202016_EN.pdf.

Environment and Climate Change Canada and Health Canada (2017). Draft screening assessment substances identified as being of low concern using the ecological risk classification of organic substances and the threshold of toxicological concern (TTC)-based approach for certain substances, June. <http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=8A598C49-1>. Accessed 4 January 2019.

Escher, B.I., Hackermüller, J., Polte, T., Scholz, S., Aigner, A., Altenburger, R., Böhme, A., Bopp, S.K., Brack, W., Busch, W., Chadeau-Hyam, M., Covaci, A., Eisenträger, A., Galligan, J.J., Garcia-Reyero, N., Hartung, T., Hein, M., Herberth, G., Jahnke, A., Kleinjans, J., Klüver, N., Krauss, M., Lamoree, M., Lehmann, I., Luckenbach, T., Müller, G.W., Müller, A., Phillips, D.H., Reemtsma, T., Rolle-Kampczyk, U., Schüürmann, G., Schwikowski, B., Tan, Y.-M., Trump, S., Walter-Rohde, S. and Wambaugh, J.F. (2017). From the exposome to mechanistic understanding of chemical-induced adverse effects. *Environment International* 99, 97-106. <https://doi.org/10.1016/j.envint.2016.11.029>.

European Chemicals Agency (2017) *Non-animal Approaches - Current Status of Regulatory Applicability Under the REACH, CLP and Biocidal Products Regulations* https://echa.europa.eu/documents/10162/22931011/non_animal_approaches_en.pdf/87ebb68f-2038-f597-fc33-f4003e9e7d7d.

European Chemicals Agency (n.d. a). Search for chemicals. <https://www.echa.europa.eu/information-on-chemicals>. Accessed 30 December 2018.

European Chemicals Agency (n.d. b). How to avoid unnecessary testing on animals: weight of evidence. <https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/weight-of-evidence>. Accessed 4 January 2019.

European Chemicals Agency (n.d. c). How to avoid unnecessary testing on animals: grouping of substances and read-across. <https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across>. Accessed 29 August 2018.

European Commission (2015). Exposing the exposome, 22 September. *Horizon 2020*. <https://ec.europa.eu/programmes/horizon2020/en/news/exposing-exposome>. Accessed 1 January 2019.

European Commission (2018a). Nanomaterials in REACH and CLP. http://ec.europa.eu/environment/chemicals/nanotech/reach-clp/index_en.htm. Accessed 23 August 2018.

European Commission (2018b). *Communication from the Commission to the European Parliament, the Council and the European Economic and Social Committee: General Report on the Operation of REACH and Review of Certain Elements. Conclusions and Actions*. <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=C ELEX:52018DC0116&from=EN>.

European Commission (2018c). The REACH REFIT evaluation (REACH review). https://ec.europa.eu/growth/sectors/chemicals/reach/review_en. Accessed 29 August 2018.

European Commission (2018d). Information platform for chemical monitoring: enhancing access to chemical data. Environmental Sciences Europe. <https://ipchem.jrc.ec.europa.eu>. Accessed 30 December 2018.

European Food Safety Authority (2010). Scientific Opinion on the development of specific protection goal options for environmental risk assessment of pesticides, in particular in relation to the revision of the guidance documents on aquatic and terrestrial ecotoxicology (SANCO/3268/2001 and SANCO/10329/2002). *European Food Safety Authority Journal* 8(10), 1821-1876. <https://doi.org/10.2903/j.efsa.2010.1821>.

European Food Safety Authority (2012). Scientific Opinion on exploring options for providing advice about possible human health risks based on the concept of threshold of toxicological concern (TTC). *European Food Safety Authority Journal* 10(7), 2750-2853. <https://doi.org/10.2903/j.efsa.2012.2750>.

European Food Safety Authority (2016). Guidance to develop specific protection goals options for environmental risk assessment at EFSA, in relation to biodiversity and ecosystem services. *European Food Safety Authority Journal* 14(6), 4499-4549. <https://doi.org/10.2903/j.efsa.2016.4499>.

European Food Safety Authority (n.d.). Chemical mixtures. <https://www.efsa.europa.eu/en/topics/topic/chemical-mixtures>. Accessed 29 August 2018.

Finkel, A.M. (2011). "Solution-focused risk assessment": a proposal for the fusion of environmental analysis and action. *Human and Ecological Risk Assessment: An International Journal* 17(4), 754-787. <https://doi.org/10.1080/10807039.2011.588142>.

Food and Agriculture Organization of the United Nations (2011). *One Health: Food and Agriculture Organization of the United Nations Strategic Plan*. <http://www.fao.org/docrep/014/al868e/al868e00.pdf>.

Franklin, K. (2018). EPA lays out TSCA implementation priorities, 1 November. <https://chemicalwatch.com/71532/epa-lays-out-tsca-implementation-priorities>. Accessed 4 January 2019.

Gottardo, S., Alessandrelli, M., Amenta, V., Atluri, R., Barberio, G., Bekker, C., Bergonzo, P., Bleeker, E., Booth, A.M., Borges, T., Buttolo, P., Carlander, D., Castelli, S., Chevillard, S., Clavaguera, S., Dekkers, S., Delpivo, C., Di Prospero Fanghella, P., Dusinska, M., Einola, J., Ekokoski, E., Fito, C., Gouveia, H., Grall, R., Hoehener, K. and Joh, H. (2017). *NANoREG Framework for the Safety Assessment of Nanomaterials*. Gottardo, S., Crutzen, H. and Jantunen, P. (eds.). Ispra: Joint Research Centre. <https://doi.org/10.2760/245972>.

- Government of Canada (2016a). Chemicals management plan, 2 June. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan.html>. Accessed 1 January 2019.
- Government of Canada (2016b). Chemicals management plan risk assessment toolbox, 30 May. <https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-management-plan-risk-assessment-toolbox.html>. Accessed 1 January 2019.
- Government of Canada (2017a). The identification of risk assessment priorities, 15 June. <https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/identification-risk-assessment-priorities.html>. Accessed 4 January 2019.
- Government of Canada (2017b). Application of weight of evidence and precaution in risk assessment, 15 June. <https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/application-weight-of-evidence-precaution-risk-assessments.html>. Accessed 4 January 2019.
- Government of Canada (2018a). *Chemicals Management Plan Progress Report: Summer 2018*. [https://www.canada.ca/content/dam/eccc/documents/pdf/pded/chemicals-management-plan-\(cmp\)-progress-report/cmp-progress-report-summer-2018.pdf](https://www.canada.ca/content/dam/eccc/documents/pdf/pded/chemicals-management-plan-(cmp)-progress-report/cmp-progress-report-summer-2018.pdf).
- Government of Canada (2018b). *Follow-Up Report to the House of Commons Standing Committee on Environment and Sustainable Development on the Canadian Environmental Protection Act, 1999*. Ottawa. <https://www.canada.ca/content/dam/eccc/documents/pdf/cepa/FollowUpCepaReport-eng.pdf>
- Hansen, B.G. (2017). Hazard versus risk, *Chemical Watch*, October. <https://chemicalwatch.com/60340/hazard-versus-risk>. Accessed 1 June 2018
- Human Exposome Project (2019) The exposome's 10th year in review <https://humanexposomeproject.com/news/the-exposomes-10th-year-in-review/>. Accessed 4 January 2019.
- International Chemical Secretariat (n.d.). Sin list. <http://chemsec.org/sin-list/>. Accessed 1 June 2018.
- Jabbour, J. and Flachsland, C. (2017). 40 years of global environmental assessments: a retrospective analysis. *Environmental Science & Policy* 77, 193-202. <https://doi.org/10.1016/j.envsci.2017.05.001>.
- Karmaus, A.L., Filer, D.L., Martin, M.T. and Houck, K.A. (2016). Evaluation of food-relevant chemicals in the ToxCast high-throughput screening program. *Food and Chemical Toxicology* 92, 188-196. <https://doi.org/10.1016/j.fct.2016.04.012>.
- Kortenkamp, A., Backhaus, T. and Faust, M. (2009). *State of the Art Report on Mixture Toxicity: Final Report*. Executive Summary. European Commission, DG Environment. http://ec.europa.eu/environment/chemicals/effects/pdf/report_mixture_toxicity.pdf.
- Laux, P., Tentschert, J., Riebeling, C., Braeuning, A., Creutzenberg, O., Epp, A., Fessard, V., Haas, K.-H., Haase, A., Hund-Rinke, K., Jakubowski, N., Kearns, P., Lampen, A., Rauscher, H., Schoonjans, R., Störmer, A., Thielmann, A., Mühle, U. and Luch, A. (2018). Nanomaterials: certain aspects of application, risk assessment and risk communication. *Archives of Technology* 92(1) 121-141. <https://doi.org/10.1007/s00204-017-2144-1>.
- Liu, J., Patlewicz, G., Williams A.J., Thomas R.S., and Shah I. (2017). Predicting organ toxicity using *in vitro* bioactivity data and chemical structure. *Chemical Research in Toxicology* 30(11), 2046-2059. <https://doi.org/10.1021/acs.chemrestox.7b00084>.
- Maltby, L., Jackson, M., Whale, G., Brown, A.R., Hamer, M., Solga, A., Kabouw, P., Woods, R. and Marshall, S. (2017). Is an ecosystem services-based approach developed for setting specific protection goals for plant protection products applicable to other chemicals? *Science of The Total Environment* 580, 1222-1236. <https://doi.org/10.1016/j.scitotenv.2016.12.083>.
- Meek, B., Boobis, A.R., Crofton, K.M., Heinemeyer, G., Raaij, M. Van and Vickers, C. (2011). Risk assessment of combined exposure to multiple chemicals: a WHO/IPCS framework. *Regulatory Toxicology and Pharmacology* 60(2), S1-S14. <https://doi.org/10.1016/j.yrtph.2011.03.010>.
- Milner, A.M. and Boyd, I.L. (2017). Toward pesticidevigilance. *Science* 357(6357), 1232-1234. <https://doi.org/10.1126/science.aan2683>.
- Organisation for Economic Co-operation and Development (2002) *OECD Guidance Document on Risk Communication for Chemical Risk Management*. [http://www.oecd.org/officialdocuments/publicdisplaydocumententpdf/?cote=env/jm/mono\(2002\)18&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumententpdf/?cote=env/jm/mono(2002)18&doclanguage=en)
- Organisation for Economic Co-operation and Development (2011). *WHO OECD ILSI/HESI International Workshop on Risk Assessment of Combined Exposures to Multiple Chemicals*. Workshop Report. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2011\)10&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2011)10&doclanguage=en).
- Organisation for Economic Co-operation and Development (2014). *Guidance on Grouping of Chemicals*. 2nd edn. [http://www.oecd.org/officialdocuments/publicdisplaydocumententpdf/?cote=env/jm/mono\(2014\)4&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumententpdf/?cote=env/jm/mono(2014)4&doclanguage=en).
- Organisation for Economic Co-operation and Development (2016). OECD environmental risk assessment toolkit. <https://envriskassessmenttoolkit.oecd.org/Default.aspx?idExec=c024b15b-9573-433c-a8a1-f100951a0686>. Accessed 1 January 2019.

- Organisation for Economic Co-operation and Development (2018). Grouping of chemicals: chemical categories and read-across. <http://www.oecd.org/chemicalsafety/risk-assessment/groupingofchemicalscategoriesandread-across.htm>. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (n.d.). The global portal to information on chemical substances. *eChemPortal*. <https://www.echemportal.org/echemportal/index.action>. Accessed 1 January 2019.
- Pham, N., Iyer, S., Hackett, E., Lock, B.H., Sandy, M., Zeise, L., Solomon, G. and Marty, M. (2016). Using ToxCast to explore chemical activities and hazard traits: a case study with ortho- phthalates. *Toxicological Sciences* 151(2), 286-301. <https://doi.org/10.1093/toxsci/kfw049>.
- Pleil, J. (2015). The human exposome and systems biology: ongoing empirical measurement studies and biomarker interpretation, 57 May. https://cfpub.epa.gov/si/si_public_record_report.cfm?dirEntryId=311388&Lab=NERL. Accessed 3 January 2019.
- Rhomberg, L.R., Goodman, J.E., Bailey, L.A., Prueitt, R.L., Beck, N.B., Bevan, C., Honeycutt, M., Kaminski, N.E., Paoli, G., Pottenger, L.H., Scherer, R.W., Wise, K.C. and Becker, R.A. (2013). A survey of frameworks for best practices in weight-of-evidence analyses. *Critical Reviews in Toxicology* 43(9), 753-784. <https://doi.org/10.3109/10408444.2013.832727>.
- Roth, N. and Wilks, M.F. (2014). Neurodevelopmental and neurobehavioural effects of polybrominated and perfluorinated chemicals: a systematic review of the epidemiological literature using a quality assessment scheme. *Toxicology Letters* 230(2), 271-281. <https://doi.org/10.1016/j.toxlet.2014.02.015>.
- Sahlin, U. and Rundlöf, M. (2016). Differences in the strengths of evidence matters in risk-risk trade-offs. *Journal of Risk Research* 20(8), 988-994. <https://doi.org/10.1080/13669877.2016.1178662>.
- Selin, H. (2013). Global chemicals politics and policy. In *The Handbook of Global Climate and Environment Policy*. Oxford: Wiley. 107-123. <https://doi.org/10.1002/9781118326213.ch7>.
- Shah, F. and Greene, N. (2014). Analysis of Pfizer compounds in EPA's ToxCast chemicals-assay space. *Chemical Research in Toxicology* 27(1), 86-98. <https://doi.org/10.1021/tx400343t>.
- Swedish Chemicals Agency (2018). *Grouping of Chemical Substances in the REACH and CLP Regulations*. <https://www.kemi.se/global/pm/2018/pm-2-18-grouping-of-chemical-substances-in-the-reach-and-clp-regulations1.pdf>.
- Teeguarden, J.G., Tan, Y.-M., Edwards, S.W., Leonard, J.A., Anderson, K.A., Corley, R.A., Kile, M.L., Simonich, S.M., Stone, D., Tanguay, R.L., Waters, K.M., Harper, S.L. and Williams, D.E. (2016). Completing the link between exposure science and toxicology for improved environmental health decision making: the aggregate exposure pathway framework. *Environmental Science & Technology* 50(9), 4579-4586. <https://doi.org/10.1021/acs.est.5b05311>.
- United Nations (2017). *Globally Harmonized System of Classification and Labelling of Chemicals (GHS): Health and Environmental Hazards - Classification Criteria for Substances and Mixtures*. https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/GHS_presentations/English/health_env_e.pdf.
- United Nations Office for Disaster Risk Reduction (2017). *Words into Action Guidelines: National Disaster Risk Assessment. Special Topics A. Public Communication for Disaster Risk Reduction*. [https://www.preventionweb.net/files/52828_apubliccommunication\[1\].pdf](https://www.preventionweb.net/files/52828_apubliccommunication[1].pdf).
- United States Agency for Toxic Substances and Disease Registry (2018) *Framework for Assessing Health Impacts of Multiple Chemicals and Other Stressors (Update)*. <https://www.atsdr.cdc.gov/interactionprofiles/ip-ga/ipga-p.pdf>.
- United States Centers for Disease Control and Prevention (2018). National Health and Nutrition Examination Survey. <https://www.cdc.gov/nchs/nhanes/index.htm>. Accessed 1 June 2018.
- United States Congress (2016). *The Frank R. Lautenberg Chemical Safety for the 21st Century Act. Public Law 114-182 - 114th Congress*. <https://www.congress.gov/114/plaws/publ182/PLAW-114publ182.pdf>.
- United States Environmental Protection Agency (2017). Control of nanoscale materials under the Toxic Substances Control Act, 30 November. <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/control-nanoscale-materials-under>. Accessed 14 August 2018.
- United States Environmental Protection Agency (2018a). Exploring ToxCast data: downloadable data. <https://www.epa.gov/chemical-research/exploring-toxcast-data-downloadable-data>. Accessed 1 January 2019.
- United States Environmental Protection Agency (2018b). ChemView. <https://chemview.epa.gov/chemview>. Accessed 1 June 2018.
- United States Environmental Protection Agency (2018c). CompTox chemicals dashboard: what is the comptox chemicals dashboard? 13 December. <https://www.epa.gov/chemical-research/comptox-chemicals-dashboard>. Accessed 1 January 2019.

- United States Environmental Protection Agency (2018d). *Application of Systematic Review in TSCA Evaluations*. https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tasca_05-31-18.pdf.
- United States National Academies of Sciences, Engineering and Medicine (2017). *Using 21st Century Science to Improve Risk-related Evaluations*. <https://www.nap.edu/catalog/24635/using-21st-century-science-to-improve-risk-related-evaluations>.
- United States National Research Council (2009). *Science and Decision: Advancing Risk Assessment*. <https://doi.org/10.17226/12209>.
- United States National Toxicology Program (2017). Collaborative workshop on aquatic models and 21st century toxicology, 12 December. <https://ntp.niehs.nih.gov/pubhealth/evalatm/3rs-meetings/past-meetings/aquatic-models-wksp-2014/index.html>. Accessed 1 January 2019.
- United States National Toxicology Program (2018a). OHAT systematic review, 29 January. <https://ntp.niehs.nih.gov/pubhealth/hat/review/index-2.html>. Accessed 1 January 2019.
- United States National Toxicology Program (2018b). SEAZIT: systematic evaluation of the application of zebrafish in toxicology, 30 August. <https://ntp.niehs.nih.gov/pubhealth/evalatm/test-method-evaluations/dev-tox/seazit/index.html>. Accessed 1 January 2019.
- van Broekhuizen, F.A., Posthuma L. and Traas T.P. (2016). *Addressing Combined Effects of Chemicals in Environmental Safety Assessment Under REACH – A Thought Starter*. Bilthoven: Netherlands National Institute for Public Health and the Environment. https://www.rivm.nl/en/Documents_and_publications/Scientific/Reports/2017/February/Addressing_combined_effects_of_chemicals_in_environmental_safety_assessment_under_REACH_A_thought_starter.
- van Wezel, A.P., Laak, T.L. ter, Fischer, A., Bäuerlein, P.S., Munthe, J. and Posthuma, L. (2017). Mitigation options for chemicals of emerging concern in surface waters; operationalising solutions-focused risk assessment. *Environmental Science: Water Research & Technology* 3(3), 403-414. <https://doi.org/10.1039/C7EW00077D>.
- Wang, J.C., Zhao, N.N., Chen, Y. and Li, J.H. (2015). A comparative review on chemical registration management regulations. *Applied Mechanics and Materials* 768, 820-827. <https://doi.org/10.4028/www.scientific.net/AMM.768.820>.
- Wignall, J.A., Muratov, E., Sedykh, A., Guyton, K.Z., Tropsha, A., Rusyn, I. and Chiu, W.A. (2018). Conditional toxicity value (CTV) predictor: an in silico approach for generating quantitative risk estimates for chemicals. *Environmental Health Perspectives* 126(5), 057008-1-13. <https://doi.org/10.1289/EHP2998>.
- Wilks, M.F., Roth, N., Aicher, L., Faust, M., Papadaki, P., Marchis, A., Calliera, M., Ginebreda, A., Andres, S., Kühne, R., Schüürmann, G. and HEROIC consortium. (2015). White paper on the promotion of an integrated risk assessment concept in European regulatory frameworks for chemicals. *Science of The Total Environment* 521-522, 211-218. <https://doi.org/10.1016/j.scitotenv.2015.03.065>.
- Williams, A.J., Grulke, C.M., Edwards, J., McEachran, A.D., Mansouri, K., Baker, N.C., Patlewicz, G., Shah, I., Wambaugh, J.F., Judson, R.S. and Richard, A.M. (2017). The CompTox chemistry dashboard: a community data resource for environmental chemistry. *Journal of Cheminformatics* 9(61), 1-27. <https://doi.org/10.1186/s13321-017-0247-6>.
- Woodruff, T.J. and Sutton, P. (2014). The navigation guide systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. *Environmental Health Perspectives* 122(10), 1007-1014. <https://doi.org/10.1289/ehp.1307175>.
- World Health Organization (2010). *WHO Human Health Risk Assessment Toolkit: Chemical Hazards*. http://apps.who.int/iris/bitstream/handle/10665/44458/9789241548076_eng.pdf;jsessionid=13EE48B03B976863804FF725EE3AC471?sequence=1.
- World Health Organization (2017a). *Chemical Mixtures in Source Water and Drinking-water*. <http://apps.who.int/iris/bitstream/handle/10665/255543/9789241512374-eng.pdf;jsessionid=945450215FE5D872A33483300F7FD600?sequence=1>.
- World Health Organization (2017b). One health. <http://www.who.int/features/qa/one-health/en/>. Accessed 29 August 2018.
- World Health Organization (2017c). *Guidance Document on Evaluating and Expressing Uncertainty in Hazard Characterization*. 2nd edn. <http://apps.who.int/iris/bitstream/handle/10665/259858/9789241513548-eng.pdf;jsessionid=68396397355FA003FCBB5E3A8096AA2C?sequence=1>.
- World Health Organization (2018a). Integrated risk assessment. http://www.who.int/ipcs/methods/risk_assessment/en/. Accessed 1 June 2018.
- World Health Organization (2018b). International programme on chemical safety: chemical risk assessment network. <http://www.who.int/ipcs/network/en/>. Accessed 1 June 2018.
- World Organization for Animal Health (2018). One health “at a glance”. <http://www.oie.int/en/for-the-media/onehealth/>. Accessed 29 August 2018.

Chapter 4

- Atkinson, G., Braathen, N.A., Groom, B. and Mourato, S. (2018). *Cost-Benefit Analysis and the Environment: Further Developments and Policy Use*. Paris: Organisation for Economic Development and Co-operation. <https://doi.org/10.1787/9789264085169-en>.
- Bartelings, H., Kavallari, A., van Meijl, H. and Von Lampe, M. (2016). *Estimating the Impact of Fertilizer Support Policies: A CGE approach*. Washington, D.C.: Global Trade Analysis Project. https://www.gtap.agecon.purdue.edu/resources/res_display.asp?RecordID=4901.
- Bernstein, S. and Cashore, B. (2007). Can non-state global governance be legitimate? An analytical framework. *Regulation & Governance* 1(4), 347-371. <https://doi.org/10.1111/j.1748-5991.2007.00021.x>.
- Berrone, P., Fosfuri, A., Gelabert, L. and Gomez-Mejia, L.R. (2013). Necessity as the mother of 'green' inventions: institutional pressures and environmental innovations. *Strategic Management Journal* 34(8), 891-909. <https://doi.org/10.1002/smj.2041>.
- Böcker, T. and Finger, R. (2016). European pesticide tax schemes in comparison: an analysis of experiences and developments. *Sustainability* 8(4), 1-22. <https://doi.org/10.3390/su8040378>.
- Boström, M., Börjeson, N., Gilek, M., Jönsson, A.M. and Karlsson, M. (2011). *Towards Responsible Procurement in Relation to Chemical Risks in Textiles? Findings from an Interview Study*. Huddinge: Södertörn University. <https://pdfs.semanticscholar.org/f878/613c306f2c4e44bca438c8af423bedfdb3c0.pdf>.
- Botos, Á., Graham, J.D. and Illés, Z. (2018). Industrial chemical regulation in the European Union and the United States: a comparison of REACH and the amended TSCA. *Journal of Risk Research* 1-18. <https://doi.org/10.1080/13669877.2018.1454495>.
- Buxton, L. (2016). Hoffmann-La Roche's goal to phase out SVHCs, December. *Chemical Watch*. <https://chemicalwatch.com/51621/hoffmann-la-roches-goal-to-phase-out-svhcs>. Accessed 2 January 2019.
- Canan, P., Andersen, S.O., Reichman, N. and Gareau, B. (2015). Introduction to the special issue on ozone layer protection and climate change: the extraordinary experience of building the Montreal Protocol, lessons learned, and hopes for future climate change efforts. *Journal of Environmental Studies and Sciences* 5(2), 111-121. <https://doi.org/10.1007/s13412-015-0224-1>.
- Center for International Environmental Law (2013). *Driving Innovation: How Stronger Laws Help Bring Safer Chemicals to the Market*. http://www.ciel.org/Publications/Innovation_Chemical_Feb2013.pdf.
- ChemSafetyPro (2018) GHS Classification of mixture, 17 October. https://www.chemsafetypro.com/Topics/GHS/GHS_classification_mixture.html. Accessed 2 January 2019.
- Chiu, W.A. (2017). *Chemical Risk Assessment and Translation to Socio-economic Assessments*. Paris: Organisation for Economic Co-operation and Development. <http://dx.doi.org/10.1787/a930054b-en>.
- Consultancy.uk (2017). Portfolio Sustainability Assessment gaining momentum in chemicals industry, 28 March. <https://www.consultancy.uk/news/13241/portfolio-sustainability-assessment-gaining-momentum-in-chemicals-industry>. Accessed 1 January 2019.
- Cook, G. and Jardim, E. (2017). *Guide to Greener Electronics 2017*. Bach, N. (ed.). Washington, D.C.: Greenpeace. <https://www.greenpeace.org/usa/wp-content/uploads/2017/10/Guide-to-Greener-Electronics-2017.pdf>.
- Dalvie, M.A., Rother, H.A. and London, L. (2014). Chemical hazard communication comprehensibility in South Africa: safety implications for the adoption of the globally harmonised system of classification and labelling of chemicals. *Safety Science* 61, 51-58. <https://doi.org/10.1016/j.ssci.2013.07.013>.
- Duffus, J.H., Nordberg, M. and Templeton, D.M. (2007). Glossary of terms used in toxicology, 2nd edition (IUPAC Recommendations 2007). *Pure and Applied Chemistry. The Journal of the International Union of Pure and Applied Chemistry (IUPAC)* 79(7), 1153-1344. <https://doi.org/10.1351/pac200779071153>.
- DuPont (2015). DuPont position statement: Montreal Protocol, 15 September. <http://www.dupont.com/corporate-functions/our-company/insights/articles/position-statements/articles/montreal-protocol.html>. Accessed 1 June 2018.
- Eastlake, A., Hodson, L., Geraci, C. and Crawford, C. (2012). A critical evaluation of material safety data sheets (MSDSs) for engineered nanomaterials. *Chemical Health & Safety* 19(5), 1-8. <https://doi.org/10.1016/j.jchas.2012.02.002>.
- Egeghy, P.P., Judson, R., Gangwal, S., Mosher, S., Smith, D., Vail, J. and Cohen Hubal, E.A. (2012). The exposure data landscape for manufactured chemicals. *Science of The Total Environment* 414, 159-166. <https://doi.org/10.1016/j.scitotenv.2011.10.046>.
- Egeghy, P.P., Vallero, D.A. and Cohen Hubal, E.A. (2011). Exposure-based prioritization of chemicals for risk assessment. *Environmental Science & Policy* 14(8), 950-964. <https://doi.org/10.1016/j.envsci.2011.07.010>.

- Eklund, A.G., Altshuler, S.L., Altshuler, P.C., Chow, J.C., Hidy, G.M., Lloyd, A.C., Prather, M.J., Watson, J.G., Zalzal, P., Andersen, S.O., Halberstadt, M.L. and Borgford-Parnell, N. (2013). Stratospheric ozone, global warming, and the principle of unintended consequences – an ongoing science and policy story. *Journal of the Air & Waste Management Association* 63(11), 1235-1244. <https://doi.org/10.1080/10962247.2013.847317>.
- European Chemicals Agency (2011). *Guidance on the Preparation of an Application for Authorisation*. Version 1. https://echa.europa.eu/documents/10162/13643/authorisation_application_en.pdf.
- European Chemicals Agency (2017). *Socio-economic Impacts of REACH Authorisations: A Meta-Analysis of the First 100 Applications for Authorisation*. <https://doi.org/10.2823/794664>.
- European Chemicals Agency (n.d. a). Emission scenario documents. <https://echa.europa.eu/guidance-documents/guidance-on-biocides-legislation/emission-scenario-documents>. Accessed 23 August 2018.
- European Chemicals Agency (n.d. b). Extended safety data sheets. <https://echa.europa.eu/safety-data-sheets>. Accessed 9 September 2018.
- European Chemicals Agency (n.d. c) Classification of substances and mixtures <https://echa.europa.eu/regulations/clp/classification>. Accessed 2 January 2019.
- European Chemicals Agency (n.d. d). Understanding REACH. <https://echa.europa.eu/regulations/reach/understanding-reach>. Accessed 1 June 2018.
- European Chemicals Agency (n.d. e). Regulatory management option analysis. <https://echa.europa.eu/rmoa>. Accessed 1 June 2018.
- European Commission (2015). *Monitoring the Impacts of REACH on Innovation, Competitiveness and SMEs*. <http://ec.europa.eu/DocsRoom/documents/14581/attachments/1/translations>.
- Frangos, J., D'Costa, G., Hagen, T. and Drew, R. (2010). *An Evaluation of MSDS and Labels Associated with the Use of Engineered Nanomaterials*. Canberra: Safe Work Australia. <https://www.safeworkaustralia.gov.au/system/files/documents/1702/anevaluationofmsdsandlabelsassociatedwiththeuseofengineerednanomaterials.doc>.
- Franklin, K. (2015). Trend in retailers removing phthalates from flooring continues, 16 July. *Chemical Watch*. <https://chemicalwatch.com/24489/trend-in-retailers-removing-phthalates-from-flooring-continues>. Accessed 1 June 2018.
- Franklin, K. (2016). Walmart releases high priority chemical list: substances include formaldehyde, parabens, triclosan, NPEs, phthalates, 21 July. *Chemical Watch*. <https://chemicalwatch.com/48724/walmart-releases-high-priority-chemical-list>. Accessed 9 September 2018.
- Gauthier, A.M., Fung, M., Panko, J., Kingsbury, T., Perez, A.L., Hitchcock, K., Ferracini, T., Sahmel, J., Banducci, A., Jacobsen, M., Abelmann, A. and Shay, E. (2014). Chemical assessment state of the science: evaluation of 32 decision-support tools used to screen and prioritize chemicals. *Integrated Environmental Assessment and Management* 11(2), 242-255. <https://doi.org/10.1002/ieam.1605>.
- Geiser, K. (2015) *Chemicals Without Harm: Policies for a Sustainable World*. Cambridge, MA: MIT Press. <http://mitpress.universitypressscholarship.com/view/10.7551/mitpress/9780262012522.001.0001/upso-9780262012522>.
- Government of Canada (2012). Chemicals Management Plan implementation table at a glance – 2016 to 2021, 26 July. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/implementation-table-at-a-glance-2016-2021.html>. Accessed 22 August 2018.
- Government of Canada (2016). Risk management of chemical substances: what is risk management? 4 July. <https://www.canada.ca/en/health-canada/services/chemical-substances/canada-approach-chemicals/risk-management.html>. Accessed 22 August 2018.
- GreenBiz (2018). The right chemistry. <https://www.greenbiz.com/blogs/enterprise/right-chemistry>. Accessed 1 January 2019.
- Green Chemistry and Commerce Council (n.d.). Advancing Green Chemistry across sectors and supply chains. <https://www.greenchemistryandcommerce.org/>. Accessed 2 January 2019.
- Green Science Policy Institute (2013). Pop Stop: Denmark retailer stops sale of microwave popcorn amid health fears, 3 June. <http://greensciencepolicy.org/pop-stop/>. Accessed 1 June 2018.
- GreenScreen (2018) GreenScreen for safer chemicals. <https://www.greenscreenchemicals.org/>. Accessed 9 September 2018.
- Hansen, B.G. (2017). Hazard versus risk: the difference between alternative ways of managing chemicals is actually not that large, October. *Chemical Watch*. <https://chemicalwatch.com/60340/hazard-versus-risk>. Accessed 1 January 2019.
- Hansson, S.O. (1997). Can we reverse the burden of proof? *Toxicology Letters* 90(2-3), 223-228. [https://doi.org/10.1016/S0378-4274\(96\)03851-9](https://doi.org/10.1016/S0378-4274(96)03851-9).
- Hartmann, S. and Klaschka, U. (2017). Interested consumers' awareness of harmful chemicals in everyday products. *Environmental sciences Europe* 29(1), 29. <https://doi.org/10.1186/s12302-017-0127-8>.

- Henson, S. and Humphrey, J. (2009). *The Impacts of Private Food Safety Standards on the Food Chain and on Public Standard-setting Processes*. Rome and Geneva: Food and Agriculture Organization of the United Nations and World Health Organization. <http://www.fao.org/3/a-i1132e.pdf>.
- Humphrey, J. (2017). Regulation, standards and risk management in the context of globalization. In *Regulations and International Trade: New Sustainability Challenges for East Asia*. 21-58. Michida, E., Humphrey J. and Nabeshima K. (eds.). Cham: Palgrave Macmillan. Chapter 2. 21-58. https://doi.org/10.1007/978-3-319-55041-1_2.
- International Agency for Research on Cancer (2018). Agents classified by the IARC monographs. Volumes 1-121. <https://monographs.iarc.fr/ENG/Classification/ClassificationsAlphaOrder.pdf>.
- International Chemical Trade Association (n.d.). Responsible care. <https://www.icta-chem.org/explore-topics/responsible-care>. Accessed 1 January 2019.
- International Council of Chemical Associations (2015). Responsible Care® - the quest for performance excellence. <https://www.icca-chem.org/responsible-care/>. Accessed 22 August 2018.
- International Finance Corporation (2012). *2012 Performance Standards*. https://www.ifc.org/wps/wcm/connect/topics_ext_content/ifc_external_corporate_site/sustainability-at-ifc/policies-standards/performance-standards.
- International Labour Organization (2017). C170 - Chemicals Convention, 1990 (No. 170). Convention concerning Safety in the use of Chemicals at Work. https://www.ilo.org/dyn/normlex/en/f?p=NORMLEX_PUB:12100:0::NO::P12100_ILO_CODE:C170. Accessed 23 August 2018.
- International Labour Organization (2018). International chemical safety cards. https://www.ilo.org/safework/info/publications/WCMS_113134/lang--en/index.htm. Accessed 23 August 2018.
- Jacobs, M.M., Malloy, T.F., Tickner, J.A. and Edwards, S. (2015). Alternatives assessment frameworks: research needs for the informed substitution of hazardous chemicals. *Environmental Health Perspectives* 124(3), 265-280. <https://doi.org/10.1289/ehp.1409581>.
- Lee, J.H., Kuk, W.K., Kwon, M., Lee, J.H., Lee, K.S. and Yu, I.J. (2012). Evaluation of information in nanomaterial safety data sheets and development of international standard for guidance on preparation of nanomaterial safety data sheets. *Nanotoxicology* 7(3), 338-345. <https://doi.org/10.3109/17435390.2012.658095>.
- Lofstedt, R.E. (2011). Risk versus hazard – how to regulate in the 21st century. *European Journal of Risk Regulation* (2), 149-168. <http://risksymposium.eu/wp-content/uploads/2013/06/Risk-Versus-Hazard-Prof.-Ragnar-Lofstedt.pdf>.
- Massey, R. (2008). Sharing knowledge about chemicals: policy options for facilitating information flow. In *Options for State Chemicals Policy Reform – A Resource Guide*. Coffin, M. and Dunn, M.L. (eds.). Lowell, MA: Lowell Center for Sustainable Production. Chapter 2. 69–96. <http://sustainableproduction.org/downloads/OptionsforStateChemicalsPolicyReform.pdf>.
- Maxwell, J. and Briscoe, F. (1997). There's money in the air: the CFC ban and DuPont's regulatory strategy. *Business Strategy and the Environment* 6(5), 276-286. [https://doi.org/10.1002/\(SICI\)1099-0836\(199711\)6:5<276::AID-BSE123>3.0.CO;2-A](https://doi.org/10.1002/(SICI)1099-0836(199711)6:5<276::AID-BSE123>3.0.CO;2-A).
- Milieu, T.M.C. Asser Institute and PACE (2011). *Considerations on the Application of the Precautionary Principle in the Chemicals Sector: Final Report*. Brussels: European Commission. http://ec.europa.eu/environment/chemicals/reach/pdf/publications/final_report_pp.pdf.
- Morita, T. and Morikawa, K. (2011). Expert review for GHS classification of chemicals on health effects. *Industrial Health* 49(5), 559-565. <https://doi.org/10.2486/indhealth.MS1267>.
- Nicol, A.-M., Hurrell, A.C., Wahyuni, D., McDowall, W. and Chu, W. (2008). Accuracy, comprehensibility, and use of material safety data sheets: a review. *American Journal of Industrial Medicine* 51(11), 861-876. <https://doi.org/10.1002/ajim.20613>.
- Organisation for Economic Co-operation and Development (2015). *Preliminary Analysis of Policy Drivers Influencing Decision Making in Chemicals Management*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2015\)21&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2015)21&doclanguage=en).
- Organisation for Economic Co-operation and Development (2016). *Workshop Report: OECD Workshop Report on Socioeconomic Impact Assessment of Chemicals Management*. https://echa.europa.eu/documents/10162/22816069/sea_oecd_workshop_chem_man_en.pdf/4c94f130-f04b-2c3f-ebda-55c2df236e97.
- Organisation for Economic Co-operation and Development (2018a). Emission scenario documents. <http://www.oecd.org/chemicalsafety/risk-assessment/emissionsscariodocuments.htm>. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018b). The costs and benefits of regulating chemicals. <http://www.oecd.org/chemicalsafety/risk-management/sacame.htm>. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (2018c). IOMC toolbox for decision making in chemicals management, 25 May. <https://iomctoolbox.oecd.org/Default.aspx?idExec=d39e45a0-70e0-47f4-9949-1ec46f320b1b>. Accessed 1 June 2018.

- Organisation for Economic Co-operation and Development (n.d.). Regulations and restrictions. <http://www.oecdsaatoolbox.org/Home/Regulations>. Accessed 1 January 2019.
- Panko, J., Hitchcock, K., Fung, M., Spencer, P., Kingsbury, T. and Mason, A. (2017). A comparative evaluation of five hazard screening tools. *Integrated Environmental Assessment and Management*. 13(1), 139-154. <https://doi.org/10.1002/ieam.1757>.
- Pedersen, A.B., (2016) *Pesticide Tax in Denmark*. Aarhus University and Institute for European Environmental Policy. <https://ieep.eu/uploads/articles/attachments/504788d7-db01-4dd8-bece-ee7b9e63979e/DK%20Pesticide%20Tax%20final.pdf?v=63680923242>.
- Pelkmans, J. and Renda, A. (2014). *Does EU Regulation Hinder or Stimulate Innovation?* Brussels: Centre for European Policy Studies. <https://www.ceps.eu/system/files/No%2096%20EU%20Legislation%20and%20Innovation.pdf>.
- Perlmutter, A. (2015a). *Advancing Safer Chemicals in Products: The Key Role of Purchasing*. Lowell, MA: University of Massachusetts Lowell. https://www.epa.gov/sites/production/files/2015-09/documents/uml-rpt_greenpurchasing_7_15_14-2_0.pdf.
- Perlmutter, A. (2015b). The rise of the non-toxic buyer: 6 case studies on safer chemistry, 12 November. *GreenBiz*. <https://www.greenbiz.com/article/rise-non-toxic-buyer-6-case-studies-safer-chemistry>. Accessed 1 January 2019.
- Persson, L., Karlsson-Vinkhuyzen, S., Lai, A., Persson, Å. and Fick, S. (2017). The globally harmonized system of classification and labelling of chemicals: explaining the legal implementation gap. *Sustainability* 9(12), 2176. <https://doi.org/10.3390/su9122176>.
- Rossi, M.S., Edwards, S., Peele, C. and Greiner, T. (2017). *The Chemical Footprint Project: 2017 Annual Report*. Chemical Footprint Project. <https://www.chemicalfootprint.org/info/cfp-report-2017>.
- Rother, H.-A. (2014). Communicating pesticide neurotoxicity research findings and risks to decision-makers and the public. *NeuroToxicology* 45, 327-337. <https://doi.org/10.1016/j.neuro.2014.03.001>.
- Rother, H.-A. (2018). Pesticide labels: protecting liability or health? – unpacking ‘misuse’ of pesticides. *Current Opinion in Environmental Science & Health* 4, 10-15. <https://doi.org/10.1016/j.coesh.2018.02.004>.
- Rotman, D. (2007). Remembering the Montreal Protocol, 1 January. *MIT Technology Review*. <https://www.technologyreview.com/s/407083/remembering-the-montreal-protocol/>. Accessed 2 June 2018.
- Sathar, F., Dalvie, M. and Rother, H.-A. (2016). Review of the literature on determinants of chemical hazard information recall among workers and consumers. *International Journal of Environmental Research and Public Health* 13(6), 546. <https://doi.org/10.3390/ijerph13060546>.
- Scott, J., Smith, T., Rehmatulla, N. and Milligan, B. (2017). The promise and limits of private standards in reducing greenhouse gas emissions from shipping. *Journal of Environmental Law*. 29(2), 231-262. <https://doi.org/10.1093/jel/eqw033>.
- Stockholm Environment Institute (2014). *How Far to the 2020 goal? The Strategic Approach to International Chemicals Management in Tanzania*. <https://www.sei.org/mediamanager/documents/Publications/SEI-PolicyBrief-Persson-Tanzania.pdf>.
- Stockholm Environment Institute (2017). *Reducing Chemical Risks in Low-income Countries: Strategies for Improved Coverage of Basic Chemicals-Management Legislation*. <https://f88973py3n24eoxbq1o3o0fz-wpengine.netdna-ssl.com/wp-content/uploads/2018/03/180307c-brandon-persson-chemicals-pb-1802g.pdf>.
- Stringer, L. (2018). Cross-sector initiative sets full materials disclosure goal, 14 June. *Chemical Watch*. <https://chemicalwatch.com/67695/cross-sector-initiative-sets-full-materials-disclosure-goal>. Accessed 1 January 2019.
- Ta, G.C., Mokhtar, M. Bin, Mohd Mokhtar, H.A. Bin, Ismail, A. Bin and Abu Yazid, M.F.B.H. (2010). Analysis of the comprehensibility of chemical hazard communication tools at the industrial workplace. *Industrial Health* 48(6), 835-844. <https://doi.org/10.2486/indhealth.MS1153>.
- Tan, S.S. (2005). Decreasing environmental pollution through reducing environmentally damaging subsidies: the case of agricultural input subsidies. *Journal of Administrative Science* 3(2), 207-214. <http://ybd.dergi.comu.edu.tr/dosyalar/Ybd/decreasing-environmental-pollution-through-reducing-environmentally-damagin-2017-02-13-212.pdf>.
- United Nations (1992). *Report of the United Nations Conference on Environment and Development - Annex 1: Rio Declaration on Environment and Development*. 14 June. A/CONF.151/26 (Vol. I). <https://www.un.org/documents/ga/conf151/aconf15126-1annex1.htm>. Accessed 1 January 2019.
- United Nations Economic Commission for Europe (2017). GHS presentations: Globally Harmonized System of Classification and Labelling of Chemicals (GHS). https://www.unece.org/trans/danger/publi/ghs/presentation_e.html. Accessed 1 January 2019.
- United Nations Economic Commission for Europe (n.d. a). GHS implementation. https://www.unece.org/trans/danger/publi/ghs/implementation_e.html. Accessed 1 January 2019.

- United Nations Economic Commission for Europe (n.d. b). GHS pictograms. <https://www.unece.org/trans/danger/publi/ghs/pictograms.html>. Accessed 2 June 2018.
- United Nations Environment Programme (2013). *Sustainable Public Procurement: A Global Review*. <https://globalecolabelling.net/assets/Documents/unep-spp-report.pdf>.
- United Nations Environment Programme (2015) *LIRA Guidance: UNEP Guidance on the Development of Legal and Institutional Infrastructures and Measures for Recovering Costs of National Administration for Sound Management of Chemicals*. <https://www.unenvironment.org/resources/report/lira-guidance>.
- United Nations Environment Programme (2016). The Kigali amendment to the Montreal protocol: another global commitment to stop climate change, 8 December. <https://www.unenvironment.org/news-and-stories/news/kigali-amendment-montreal-protocol-another-global-commitment-stop-climate>. Accessed 1 January 2019.
- United Nations Environment Programme (2018). OzonAction: national ozone unit contacts, November. <http://web.unep.org/ozonaction/resources/national-ozone-unit-contacts>. Accessed 1 January 2019.
- United States Centers for Disease Control and Prevention (2015). Hierarchy of controls, 13 January. <https://www.cdc.gov/niosh/topics/hierarchy/default.html>. Accessed 1 January 2019.
- United States Environmental Protection Agency (2016). Benefits of addressing HFCs under the Montreal Protocol, 20 July. <https://www.epa.gov/ozone-layer-protection/benefits-addressing-hfcs-under-montreal-protocol>. Accessed 1 January 2019.
- United States Environmental Protection Agency (2018). Guidelines for preparing economic analyses, 31 January. <https://www.epa.gov/environmental-economics/guidelines-preparing-economic-analyses>. Accessed 1 January 2019.
- United States National Aeronautics and Space Administration (2015). NASA study shows that common coolants contribute to ozone depletion, 22 October. <https://www.nasa.gov/press-release/goddard/nasa-study-shows-that-common-coolants-contribute-to-ozone-depletion>. Accessed 1 January 2019.
- United States Occupational Safety and Health Administration (2012). Hazard communication standard: safety data sheets. <https://www.osha.gov/Publications/OSHA3514.html>. Accessed 1 January 2019.
- United States Occupational Safety and Health Administration (2013). *Hazard Communication Standard: Labels and Pictograms*. <https://www.osha.gov/Publications/OSHA3636.pdf>.
- Videras, J. and Alberini, A. (2007). The appeal of voluntary environmental programs: which firms participate and why? *Contemporary Economic Policy*. 18(4), 449-460. <https://doi.org/10.1111/j.1465-7287.2000.tb00041.x>.
- Wang, Y., Wu, E., Gao, X. and Ding, Q. (2016). Global governance on chemical sound management and challenges in Asia-Pacific region. *Procedia Environmental Sciences* 31, 911-916. <https://doi.org/10.1016/J.PROENV.2016.02.109>.
- World Business Council for Sustainable Development (2015). *Towards a Social Capital Protocol: A Call for Collaboration*. <https://www.wbcsd.org/Programs/People/Social-Impact/Resources/Towards-a-Social-Capital-Protocol-A-Call-for-Collaboration>.
- World Business Council for Sustainable Development (2018). WBCSD launches first-of-its-kind guidance for the chemical industry to assess sustainability across its product portfolio, 17 April. <https://www.wbcsd.org/Programs/Circular-Economy/Factor-10/Sector-Deep-Dives/News/guidance-for-the-chemical-industry-to-assess-sustainability-across-its-product-portfolio>. Accessed 1 January 2019.
- World Health Organization (WHO) (2017). *WHO Guidelines on Protecting Workers from Potential Risks of Manufactured Nanomaterials*. <http://apps.who.int/iris/bitstream/handle/10665/259671/9789241550048-eng.pdf;jsessionid=2FD1722707BDE8E98B9B1D9F345DE46E?sequence=1>.
- World Health Organization (2018a). International Programme on Chemical Safety: International Chemical Safety Cards. <http://www.who.int/ipcs/publications/icsc/en/>. Accessed 3 January 2019.
- World Health Organization (2018b). The Inter-Organization Programme for the Sound Management of Chemicals. <http://www.who.int/iomc/en/>. Accessed 1 January 2019.
- Zhu, J., Liu, J.G., Hu, J. And Yi, S. (2016). Socio-economic analysis of the risk management of hexabromocyclododecane (HBCD) in China in the context of the Stockholm Convention. *Chemosphere* 150, 520-527. <https://doi.org/10.1016/j.chemosphere.2015.11.007>.

Chapter 5

- Anastas, P.T., Constable, D.J.C. and Jiménez-González, C.C. (eds.) (2018). *Green Metrics. Handbook of Green Chemistry series*. Wiley-VCH. <https://www.wiley.com/en-ch/Green+Metrics,+Volume+11-p-9783527695270>.
- Ashford, N.A. (2013). Reducing physical hazards: encouraging inherently safer production. In *Designing Safer Chemicals. Handbook of Green Chemistry*. Anastas, P. T., Boethling, R. and Votchkova, A. (eds). Weinheim: John Wiley & Sons. Chapter 17. 485-500. <https://doi.org/10.1002/9783527628698.hgc111>.

- Babrauskas, V., Lucas, D., Eisenberg, D., Singla, V., Dedeo, M. and Blum, A. (2012). Flame retardants in building insulation: a case for re-evaluating building codes. *Building Research & Information* 40(6), 738-755. <https://doi.org/10.1080/09613218.2012.744533>.
- Baker, M. (2018). Despite bans, toxic flame retardants continue to show up in pregnant women's blood, 5 February. *University of California San Francisco News Center*. <https://www.ucsf.edu/news/2018/02/409746/toxic-flame-retardants-continue-show-up-pregnant-women>. Accessed 30 August 2018.
- Birnbaum, L.S. and Bergman, A. (2010). Brominated and chlorinated flame retardants: the San Antonio statement. *Environmental Health Perspectives* 118(12), A514-A515. <https://doi.org/10.1289/ehp.1003088>.
- Brown-West, B. (2017). Walmart takes bold steps towards safer chemicals, 27 September. *GreenBiz*. <https://www.greenbiz.com/article/walmart-takes-bold-steps-towards-safer-chemicals>. Accessed 1 January 2019.
- Burgos-Hernandez, M. (2009). *Strategy for Mercury Elimination in Public Hospitals of Sonora State, Mexico: Implementation of Two Research Projects for the Achievement of a Collaborative Agreement*. Lowell, MA: University of Massachusetts Lowell, ProQuest Dissertations Publishing. <https://search.proquest.com/docview/304916652/fulltextPDF/28B244F47EA84E42PQ/1?accountid=28970>.
- Canadian Centre for Occupational Health and Safety (2017). OHS answers fact sheets: trichloroethylene, 3 January. https://www.ccohs.ca/oshanswers/chemicals/chem_profiles/trichloroethylene.html. Accessed 30 August 2018.
- Chao, E.L. and Henshaw, J.L. (2003). Methylene chloride. <https://www.osha.gov/Publications/osha3144.html>. Accessed 1 January 2019.
- Clean Production Action (2017). *GreenScreen® for Safer Chemicals Hazard Assessment Guidance, Version 1.3*. 2nd edn. [https://www.greenscreenchemicals.org/static/ee_images/uploads/resources/GreenScreen_Guidance_v1.3\(2e\)_Feb_2017_final.pdf](https://www.greenscreenchemicals.org/static/ee_images/uploads/resources/GreenScreen_Guidance_v1.3(2e)_Feb_2017_final.pdf).
- Damalas, C.A. and Koutroubas, S.D. (2018). Current status and recent developments in biopesticide use. *Agriculture* 8(1), 1-6. <https://doi.org/10.3390/agriculture8010013>.
- Data Commons (n.d.). Find healthier substances. <https://commons.healthymaterials.net/>. Accessed 17 November 2018.
- Eladak, S., Grisin, T., Moison, D., Guerquin, M.-J., N'Tumba-Byn, T., Pozzi-Gaudin, S., Benachi, A., Livera, G., Rouiller-Fabre, V. and Habert, R. (2015). A new chapter in the bisphenol A story: bisphenol S and bisphenol F are not safe alternatives to this compound. *Fertility and Sterility* 103(1), 11-21. <https://doi.org/10.1016/j.FERTNSTERT.2014.11.005>.
- European Chemicals Agency (2011). *Guidance on the Preparation of an Application for Authorisation. Version 1*. https://echa.europa.eu/documents/10162/13643/authorisation_application_en.pdf.
- European Chemicals Agency (2013). *Evaluation of New Scientific Evidence concerning DINP and DIDP: In Relation to Entry 52 of Annex XVII to REACH Regulation (EC) No 1907/2006. Final Review Report*. <https://echa.europa.eu/documents/10162/31b4067e-de40-4044-93e8-9c9ff1960715>.
- European Chemicals Agency (2014). Updated guidance on the preparation of an Annex XV dossier for the identification of substances of very high concern, 12 February. https://echa.europa.eu/de/view-article/-/journal_content/title/updated-guidance-on-the-preparation-of-an-annex-xv-dossier-for-the-identification-of-substances-of-very-high-concern. Accessed 30 August 2018.
- European Chemicals Agency (2018). *Strategy to Promote Substitution to Safer Chemicals through Innovation*. https://echa.europa.eu/documents/10162/2792271/mb_58_2017_2_annex_strategy_substitution_safer_alternatives_en.pdf/d1c31c63-4047-e7be-75d1-12320a4a8489.
- European Commission (2006). Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the registration, evaluation, authorization and restriction of chemicals (REACH), establishing a European chemicals agency, amending directive 1999/4. *Official Journal of the European Union* L(136), 3-281. <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:136:0003:0280:en:PDF>.
- European Commission (2017). *Impacts of REACH Authorisation – Final Report*. <http://ec.europa.eu/docsroom/documents/26847>.
- Fantke, P. and Ernstoff, A. (2018). LCA of chemicals and chemical products. In *Life Cycle Assessment*. Hauschild, M.Z., Rosenbaum, R.K. and Olsen, S.I. (eds.). Cham: Springer. Chapter 31. 783-815. https://doi.org/10.1007/978-3-319-56475-3_31.
- Finkbeiner, M., Ackermann, R., Bach, V., Berger, M., Brankatschk, G., Chang, Y.-J., Grinberg, M., Lehmann, A., Martínez-Blanco, J., Minkov, N., Neugebauer, S., Scheumann, R., Schneider, L. and Wolf, K. (2014). Challenges in life cycle assessment: an overview of current gaps and research needs. In *Background and Future Prospects in Life Cycle Assessment*. Klöpffer, W. (ed.). Dordrecht: Springer. Chapter 7. 207-258. https://doi.org/10.1007/978-94-017-8697-3_7.
- Fisher, J., Varenne, B., Narvaez, D. and Vickers, C. (2018). The Minamata Convention and the phase down of dental amalgam. *Bulletin of the World Health Organization* 96(6), 436-438. <https://doi.org/10.2471/BLT.17.203141>.

- Geiser, K., Tickner, J., Edwards, S. and Rossi, M. (2015). The architecture of chemical alternatives assessment. *Risk Analysis* 35(12), 2152-2161. <https://doi.org/10.1111/risa.12507>.
- González, J.M.F. (2016). *Análisis y Diagnóstico de Políticas Agroambientales en Cuba: Fortalecimiento de las Políticas Agroambientales en los Países de América Latina y el Caribe Proyecto GCP/RLA/195/BRA*. Havana: Food and Agriculture Organization of the United Nations. <http://www.fao.org/3/a-i5559s.pdf>.
- Government of Canada (2018). Combined government discussion paper and science committee report on informed substitution, 28 August. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/science-committee/meeting-records-reports/combined-government-discussion-paper-science-committee-report-informed-substitution.html>. Accessed 1 January 2019.
- Grappi, S., Romani, S. and Barbarossa, C. (2017). Fashion without pollution: how consumers evaluate brands after an NGO campaign aimed at reducing toxic chemicals in the fashion industry. *Journal of Cleaner Production* 149, 1164-1173. <https://doi.org/10.1016/j.jclepro.2017.02.183>.
- Greenpeace International (2018). Destination zero: seven years of detoxing the clothing industry, 12 July. <https://www.greenpeace.org/international/publication/17612/destination-zero/>. Accessed 30 August 2018.
- Harney, J., Nemhauser, J., Reh, C. and Trout, D. (2003). *NIOSH Health Hazard Evaluation Report: HETA #99-0260-2906*. Cincinnati: National Institute for Occupational Safety and Health. <https://www.cdc.gov/niosh/hhe/reports/pdfs/1999-0260-2906.pdf>
- Hartmann, S. and Klaschka, U. (2017). Interested consumers' awareness of harmful chemicals in everyday products. *Environmental Sciences Europe* 29(1), 29. <https://doi.org/10.1186/s12302-017-0127-8>.
- Health Care Without Harm (2018). Switching to alternatives. <https://noharm-global.org/issues/global/switching-alternatives>. Accessed 1 January 2019.
- Hogue, C. (2013). Assessing alternatives to toxic chemicals: governments, businesses, and now the National Academy of Sciences consider how to avoid "regrettable substitution". *Chemical and Engineering News* 91(50), 19-20. <https://cen.acs.org/articles/91/i50/Assessing-Alternatives-Toxic-Chemicals.html>.
- Ichihara, G., Kitoh, J., Li, W., Ding, X., Ichihara, S. and Takeuchi, Y. (2012). Neurotoxicity of 1-bromopropane: evidence from animal experiments and human studies. *Journal of Advanced Research* 3(2), 91-98. <https://doi.org/10.1016/j.jare.2011.04.005>.
- Intergovernmental Forum on Chemical Safety (2008). *Sixth Session of the Intergovernmental Forum on Chemical Safety – Final Report*. http://www.who.int/ifcs/documents/forums/forum6/f6_finalreport_en.pdf.
- International Organisation for Biological Control, International Biocontrol Manufacturers Association and Pesticide Action Network (2015). *Integrated Pest Management: Working with Nature*. <https://www.pan-europe.info/sites/pan-europe.info/files/public/resources/reports/integrated-pest-management-working-with-nature.pdf>.
- Israel, B. (2013). California to unveil new flammability standard to avoid chemicals in furniture: the new rules would cut down on the use of flame retardants that have been linked to human health effects, 8 February. *Scientific American*. <https://www.scientificamerican.com/article/california-to-unveil-new-flammability-standard-to-avoid-chemicals-in-furniture/>. Accessed 1 January 2019.
- Jacobs, M.M., Massey, R.I., Tenney, H. and Harriman, E. (2014). Reducing the use of carcinogens: the Massachusetts experience. *Reviews on Environmental Health* 29(4), 319-340. <https://doi.org/10.1515/reveh-2014-0048>.
- Jacobs, M.M., Malloy, T.F., Tickner, J.A. and Edwards, S. (2015). Alternatives assessment frameworks: research needs for the informed substitution of hazardous chemicals. *Environmental Health Perspectives* 124(3), 265-280. <https://doi.org/10.1289/ehp.1409581>.
- Jamarani, R., Erythropel, H., Nicell, J., Leask, R. and Marić, M. (2018). How green is your plasticizer? *Polymers* 10(8), 834-851. <https://doi.org/10.3390/polym10080834>.
- Lavoie, E.T., Heine, L.G., Holder, H., Rossi, M.S., Lee, R.E., Connor, E.A., Vrabel, M.A., DiFiore, D.M. and Davies, C.L. (2010). Chemical alternatives assessment: enabling substitution to safer chemicals. *Environmental Science & Technology* 44(24), 9244-9249. <https://doi.org/10.1021/es1015789>.
- MacCarthy, L. (2017). Target to remove harmful chemicals from products, invest in green chemistry, 26 January. *Sustainable Brands*. <https://sustainablebrands.com/read/product-service-design-innovation/target-to-remove-harmful-chemicals-from-products-invest-in-green-chemistry>https://www.sustainablebrands.com/news_and_views/products_design/libby_maccarthy/target_commits_remove_harmful_chemicals_products_inve. Accessed 1 January 2019.
- O'Brien, M. (2000). *Making Better Environmental Decisions: An Alternative to Risk Assessment*. Cambridge, MA: MIT Press. <https://mitpress.mit.edu/books/making-better-environmental-decisions>.
- Office of Technical Assistance and Technology (2015). *Shawmut Corporation Eliminating TCE Use by Switching to a Hot-Melt Adhesive Process*. https://www.turi.org/TURI_Publications/Case_Studies/Coatings/Shawmut_Corporation_OTA_2015.

- Organisation for Economic Co-operation and Development (2018). eChemPortal: global portal to information on chemical substances. <http://www.oecd.org/chemicalsafety/risk-assessment/echempportalglobalportaltoinformationonchemicalsubstances.htm>. Accessed 1 January 2019.
- Organisation for Economic Co-operation and Development (n.d). OECD substitution and alternatives assessment toolbox. <http://www.oecdsatoolbox.org/>. Accessed 1 January 2019.
- Persistent Organic Pollutants Review Committee (2012). *Evaluation of Non-Chemical Alternatives to Endosulfan*. Geneva: Secretariat of the Stockholm Convention. <http://synergies.pops.int/2013COPsExCOPs/Documents/tabid/2915/language/en-US/Default.aspx>.
- Pesticide Action Network UK (2017). Phasing out HHPs in Costa Rica. <http://www.pan-uk.org/phasing-out-hhps-costa-rica/>. Accessed 17 February 2019.
- Rochester, J.R. and Bolden, A.L. (2015). Bisphenol S and F: a systematic review and comparison of the hormonal activity of bisphenol A substitutes. *Environmental Health Perspectives* 123(7), 643-50. <https://doi.org/10.1289/ehp.1408989>.
- Sackmann, K., Reemtsma, T., Rahmberg, M. and Bunke, D. (2018). Impact of European chemicals regulation on the industrial use of plasticizers and patterns of substitution in Scandinavia. *Environment International* 119, 346-352. <https://doi.org/10.1016/j.envint.2018.06.037>.
- Secretariat of the Stockholm Convention (2013). Sixth meeting of the Conference of the Parties to the Stockholm Convention: decisions, 10 May. <http://chm.pops.int/TheConvention/ConferenceoftheParties/Meetings/COP6/tabid/3074/mctl/ViewDetails/EventModID/870/EventID/396/xmid/10240/Default.aspx>. Accessed 1 January 2019.
- Secretariat of the Strategic Approach to International Chemicals Management (2015). *Report of the International Conference on Chemicals Management on the Work of its Fourth Session*. http://www.saicm.org/Portals/12/documents/meetings/ICCM4/doc/K1606013_e.pdf.
- Siddiqi, M.A., Laessig, R.H. and Reed, K.D. (2003). Polybrominated diphenyl ethers (PBDEs): new pollutants – old diseases. *Clinical Medicine & Research* 1(4), 281-90. <https://doi.org/10.3121/cmr.1.4.281>.
- Sinsheimer, P. (2010). *Developing Regulatory Methods for Integrating Life Cycle Assessment into Alternatives Analysis for Identifying Safer Substitutes for Hazardous Products*. Oakland, CA: State of California Department of Toxic Substances Control. <https://www.dtsc.ca.gov/upload/sinsheimer.pdf>.
- State of California Department of Consumer Affairs. (2014). *Technical Bulletin 117-2013: Requirements, Test Procedure and Apparatus for Testing the Smolder Resistance of Materials Used in Upholstered Furniture*. <https://myhfa.org/wp-content/uploads/2014/03/TB117-2013-QA.pdf>.
- State of California Department of Toxic Substances Control (2009). *Topic 4: Alternatives Assessment with Life Cycle Thinking*. <https://dtsc.ca.gov/SCP/GRSP/upload/Alternatives-Analysis.pdf>.
- State of California Department of Toxic Substances Control (2012). *Division 4.5, Title 22, California Code of Regulations Chapter 55: California Safer Consumer Products*. <http://www.dtsc.ca.gov/LawsRegsPolicies/Regs/upload/Text-of-Final-Safer-Consumer-Products-Regulations-2.pdf>.
- State of California Department of Toxic Substances Control (2017). Alternatives analysis guide, version 1.0. <http://www.dtsc.ca.gov/SCP/AlternativesAnalysisGuidance.cfm>. Accessed 4 June 2018
- Sturcken, E. (2017). Walmart effect: retailers lead the way on chemical safety at a critical time, 10 October. *Environmental Defense Fund*. <https://www.edf.org/blog/2017/10/10/walmart-effect-retailers-lead-way-chemical-safety-critical-time>. Accessed 1 January 2019.
- SUBSPORT (n.d.). SUBSPORT: substitution support portal. <https://www.subsport.eu/>. Accessed 1 January 2019.
- Tickner, J.A., Geiser, K., Rudisill, C. and Schifano, J.N. (2013). Alternatives assessment in regulatory policy: history and future directions. In *Chemical Alternatives Assessments*. Hester, R.E. and Harrison, R.M. (eds.). Cambridge: Royal Society of Chemistry. Chapter 11. 256-295. <https://doi.org/10.1039/9781849737234-00256>.
- Tickner, J.A., Schifano, J.N., Blake, A., Rudisill, C. and Mulvihill, M.J. (2015). Advancing safer alternatives through functional substitution. *Environmental Science & Technology* 49(2), 742-749. <https://doi.org/10.1021/es503328m>.
- Tickner, J.A. and Jacobs, M. (2016). *Improving the Identification, Evaluation, Adoption and Development of Safer Alternatives: Needs and Opportunities to Enhance Substitution Efforts within the Context of REACH*. Lowell, MA: University of Massachusetts Lowell. https://echa.europa.eu/documents/10162/13630/substitution_capacity_lisp_en.pdf.
- Tickner, J.A., Jacobs, M., Malloy, T., Buck, T., Stone, A., Blake, A. and Edwards, S. (2018). Advancing alternatives assessment for safer chemical substitution: a research and practice agenda. *Integrated Environmental Assessment and Management*. <https://doi.org/10.1002/ieam.4094>.

- Tomar, R.S., Budroe, J.D. and Cendak, R. (2013). *Evidence on the Carcinogenicity of Diisonoyl Phthalate (DINP)*. Sacramento, CA: California Environmental Protection Agency. <https://oehha.ca.gov/media/downloads/proposition-65/chemicals/dinphid100413.pdf>.
- Toxics Use Reduction Institute (2013). *The Commons Principles for Alternatives Assessment: Addressing Chemicals of Concern to Human Health or the Environment*. https://www.turi.org/TURI_Publications/TURI_Chemical_Fact_Sheets/Commons_Principles_for_Alternatives_Assessment.
- Toxics Use Reduction Institute (2017). *Toxics Use Reduction and Resource Conservation: Competitiveness Impacts for Massachusetts Businesses*. https://www.turi.org/TURI_Publications/TURI_Reports/Competitiveness_Impacts_for_Massachusetts_Businesses/Toxics_Use_Reduction_and_Resource_Conservation_Competitiveness_impacts_for_Massachusetts_Businesses.
- United Nations Environment Programme (2014). *Phasing-out Methyl Bromide in Developing Countries: A Success Story and its Challenges*. http://www.unep.fr/ozonaction/information/mmcfiles/7674-e-Phasing-out_methyl_bromide_in_developing_countries.pdf.
- United Nations Environment Programme (2016). *Lessons from Countries Phasing Down Dental Amalgam Use*. <https://wedocs.unep.org/bitstream/handle/20.500.11822/11624/Dental.Amalgam.10mar2016.pages.WEB.pdf?sequence=1&isAllowed=y>.
- United Nations Environment Programme (2017). Life cycle initiative. <https://www.lifecycleinitiative.org/>. Accessed 1 January 2019.
- United Nations Environment Programme and World Health Organization (2014). *Promoting the Phase Down of Dental Amalgam in Developing Countries*. https://wedocs.unep.org/bitstream/handle/20.500.11822/13865/dental_mercury_phase_down_project_brochure_FINAL_lr.pdf?sequence=1&isAllowed=y.
- United Nations Industrial Development Organization (2018). National cleaner production centres (NCPCs) and networks. <https://www.unido.org/our-focus/cross-cutting-services/partnerships-prosperity/networks-centres-forums-and-platforms/national-cleaner-production-centres-ncpcs-networks>. Accessed 31 August 2018.
- United States Centers for Disease Control and Prevention (2008). Neurologic illness associated with occupational exposure to the solvent 1-bromopropane – New Jersey and Pennsylvania, 2007-2008. *Morbidity and Mortality Weekly Report* 57(48), 1300-1302. <http://www.ncbi.nlm.nih.gov/pubmed/19052528>.
- United States Environmental Protection Agency (2017). Design for the environment programs, initiatives and projects, 19 April. <http://www.epa.gov/saferchoice/design-environment-programs-initiatives-and-projects>. Accessed 1 January 2019.
- United States Environmental Protection Agency (2018) CompTox chemicals dashboard: what is the comptox chemicals dashboard? 13 December. <https://www.epa.gov/chemical-research/comptox-chemicals-dashboard>. Accessed 1 January 2019.
- United States National Research Council (2014). *A Framework to Guide Selection of Chemical Alternatives*. Washington, DC: National Academies Press. <http://www.nap.edu/catalog/18872>.
- United States National Toxicology Program (2011). *Toxicology and Carcinogenesis Studies of 1-bromopropane in F344/N Rats and B6C3F1 Mice (Inhalation Studies)*. Durham, NC: US Department of Health and Human Services. <https://ntp.niehs.nih.gov/results/pubs/longterm/reports/longterm/tr500580/listedreports/tr564/index.html>.
- United States Natural Resources Defense Council (2018). The Home Depot to be third major U.S. retailer to ban deadly paint strippers, 19 June. <https://www.nrdc.org/media/2018/180619>. Accessed 30 August 2018.
- United States Occupational Safety and Health Administration (n.d.). Transitioning to safer chemicals: a toolkit for employers and workers. https://www.osha.gov/dsg/safer_chemicals/index.html. Accessed 1 January 2019.
- Walmart (2018). Walmart commitment to sustainable chemistry. <https://www.walmartsustainabilityhub.com/sustainable-chemistry/sustainable-chemistry-policy>. Accessed 1 January 2019.
- Weber, R., Fantke, P., Hamouda, A. Ben and Mahjoub, B. (2018). *20 Case Studies on How to Prevent the Use of Toxic Chemicals Frequently Found in the Mediterranean Region*. Barcelona: Regional Activity Centre for Sustainable Consumption and Production (SCP/RAC). <http://www.cprac.org/en/news-archive/general/we-are-surrounded-by-toxic-chemicals-scp/rac-provides-20-case-studies-to-preven>.
- Wendschlag, H. (2015). *Business Guide to Safer Chemicals in the Supply Chain Including Alternatives Assessment*. Shrewsbury: Chemical Watch. https://www.greenscreenchemicals.org/static/ee_images/uploads/resources/HP_GREEN_SCREEN_ARTICLE.pdf.
- World Health Organization (2015). *Developing National Strategies for Phasing Out Mercury Containing Thermometers and Sphygmomanometers in Health Care, Including in the Context of the Minamata Convention on Mercury: Key Considerations and Step-by-Step Guidance*. <http://apps.who.int/iris/bitstream/handle/10665/259448/9789241508339-eng.pdf;jsessionid=A8006FEAC3880B70D81CA55703F711E1?sequence=1>.

Chapter 6

Abu Bakar, H.T., Han Siong, P., Koy Yan, C., Kidam, K., Wijayanuddin Ali, M., Hassim, M.H. and Kamarden, H. (2017). Analysis of main accident contributor according to process safety management elements failure. *Chemical Engineering Transactions* 56, 991-996. <https://doi.org/10.3303/CET1756166>.

Ahmad, I., Rehan, M., Balkhyour, M., Abbas, M., Basahi, J., Balkhyour, M.A., Basahi, J.M., Almeelbi, T. and Ismail, I.M.I. (2016). Review of environmental pollution and health risks at motor vehicle repair workshops: challenges and perspectives for Saudi Arabia. *International Journal of Agricultural and Environmental Research* 2(1), 1-23. <https://pdfs.semanticscholar.org/f80b/9eaaa61f97b2f5320d9073050f838c575b03.pdf>.

Alfers, L. (2013). *The Ghana National Health Insurance Scheme: Barriers to Access to Informal Workers*. WIEGO Working Paper (Social Protection) No. 30. Cambridge, MA and London: Women in Employment Globalizing and Organizing. <http://www.wiego.org/sites/default/files/publications/files/Alfers-Ghana-Health-Insur-Infomral-Workers-WIEGO-WP30.pdf>.

Alfers, L., Lund, F. and Moussié (2018). *Informal Workers & The Future of Work: A Defence of Work-Related Social Protection*. WIEGO Working Paper No. 37. Manchester: Women in Employment Globalizing and Organizing. http://www.wiego.org/sites/default/files/publications/files/Alfers_Informal_Workers_Social_Protection_WIEGO_WP37.pdf.

Baranzini, D., Wood, M., Krausmann, E. and Van Wijk, L. (2018). Capacity building measures for chemical accident prevention and preparedness: benchmark of EU neighbourhood countries. *International Journal of Disaster Risk Reduction* 31, 770-780. <https://doi.org/10.1016/j.ijdrr.2018.07.023>.

Benjamin, N., Beegle, K., Recanatini, F. and Santini, M. (2014). *Informal Economy and the World Bank*. Policy Research Working Paper No. 6888. Washington, D.C.: The World Bank. <http://documents.worldbank.org/curated/en/416741468332060156/pdf/WPS6888.pdf>.

Bhandubanyong, P. and Pearce, T.H. (2017). Appraisal of SME casting industry in Thailand. *International Scientific Journal of Engineering and Technology* 1(1), 1-8. http://www.responsiblemines.org/wp-content/uploads/2018/05/059_ASGM-Formalization.pdf.

Center for Chemical Process Safety (2017). Pre-conference course: CCPS overview of risk based process safety, 11 September. <https://www.aisc.org/ccps/conferences/ccps-global-summit-on-process-safety/2017/events/ccps-overview-risk-based-process-safety>. Accessed 2 June 2018.

Chakraborty, P., Selvaraj, S., Nakamura, M., Balasubramanian, P., Cincinelli, A. and Bang, J. (2018). PCBs and PCDD/Fs in soil from informal e-waste recycling sites and open dumpsites in India: levels, congener profiles and health risk assessment. *Science of the Total Environment* 621, 930-938. <https://doi.org/10.1016/j.scitotenv.2017.11.083>.

Charmes, J. (2012). The informal economy worldwide: trends and characteristics. *Margin: The Journal of Applied Economic Research* 6(2), 103-132. <https://doi.org/10.1177/097380101200600202>.

de Haan, J. and Turner, B. (2018). *Handbook: Developing National ASGM Formalization Strategies within National Action Plans*. Geneva: United Nations Institute for Training and Research and United Nations Environment Programme. https://unitar.org/cwm/sites/unitar.org/cwm/files/uploads/formalization_handbook_e_web_final.pdf.

European Commission (2017) Major accident hazards: the Seveso Directive – technological disaster reduction, 24 August. <http://ec.europa.eu/environment/seveso/index.htm>. Accessed 28 December 2018.

European Commission Joint Research Centre and United Nations Economic Commission for Europe (2016). *An Overview of Methodologies for Hazard Rating of Industrial Sites*. https://minerva.jrc.ec.europa.eu/en/shorturl/minerva/jrc101613engfinal_hazard_rating_guide3nov_2016onlinepdf.

Girgin, S., Necci, A. and Krausmann, E. (2017). Natech hazard and risk assessment. In *Words into Action Guidelines: National Disaster Risk Assessment Hazard Specific Risk Assessment*. Geneva: United Nations Office for Disaster Risk Reduction. Chapter 9. 91-98. https://www.unisdr.org/files/52828_09natechazardandriskassessment.pdf.

Gori, A., Gidaris, I., Elliott, J.R., Padgett, J., Loughran, K., Bedient, P.B., Panakkal, P. and Juan, A. (2018). NH33D-1038: investigating flood-induced cascading impacts to Houston's road network and emergency service accessibility during Hurricane Harvey. *American Geophysical Union Fall Meeting*. <https://agu.confex.com/agu/fm18/meetingapp.cgi/Paper/438218>. Accessed 28 December 2018.

Gyenes, Z. and Wood, M.H. (2014). *Lessons Learned from Major Accidents Having Significant Impact on the Environment*. Symposium Series No 159, Hazards 24. Edinburgh: Institute of Chemical Engineers. <https://doi.org/10.13140/2.1.2897.6005>.

Hassan, S.A. (2012). *Health, Safety and Environmental Practices in the Construction Sector of Pakistan*. Uppsala: Uppsala University. <http://www.diva-portal.org/smash/get/diva2:562426/FULLTEXT01.pdf>.

He, G., Zhang, L., Lu, Y. and Mol, A.P.J. (2011). Managing major chemical accidents in China: towards effective risk information. *Journal of Hazardous Materials* 187(1-3), 171-181. <https://doi.org/10.1016/j.jhazmat.2011.01.017>.

- He, Q.S. and Yang, Y.Y. (2012). Effect of EU environmental directives on chemical industries in Zhejiang. *Chemical Industry Times* 24, 75-77. https://www.researchgate.net/publication/285686566_Effect_of_EU_environmental_directives_on_chemical_industries_in_Zhejiang.
- Heikkilä, A.-M., Malmén, Y., Nissilä, M. and Kortelainen, H. (2010). Challenges in risk management in multi-company industrial parks. *Safety Science* 48(4), 430-435. <https://doi.org/10.1016/j.ssci.2009.12.008>.
- Holmes, R. and Scott, L. (2016). *Extending Social Insurance to Informal Workers: A Gender Analysis*. ODI Working Paper 438. London: Overseas Development Institute. <https://www.odi.org/sites/odi.org.uk/files/resource-documents/10620.pdf>.
- Hong, K.T., Surlenty, L. and Hung, K.M. (2011). Occupational safety and health (OHS) in Malaysian Small and Medium Enterprise (SME) and effective safety management practices. *International Journal of Business and Technopreneurship* 1(2), 321-338. https://www.researchgate.net/publication/315765815_Occupational_Safety_and_Health_OSH_in_Malaysian_Small_and_Medium_Enterprise_SME_and_Effective_Safety_Management_Practices.
- Inter-Agency Coordination Group for Industrial and Chemical Accidents (2017). *International Efforts for Industrial and Chemical Accidents Prevention, Preparedness and Response*. <https://www.oecd.org/chemicalsafety/chemical-accidents/Brochure-International-efforts-for-industrial-and-chemical-accidents.pdf>.
- International Atomic Energy Agency (2006). *IAEA Safety Standards for Protecting People and the Environment: Application of the Management System for Facilities and Activities*. https://www-pub.iaea.org/mtcd/publications/pdf/pub1253_web.pdf.
- International Institute for Environment and Development (2018). Addressing risks facing informal workers, April. <https://www.iied.org/addressing-risks-facing-informal-workers>. Accessed 27 December 2018.
- International Labour Organization (1997). Social Security for the Informal Sector: Investigating the Feasibility of Pilot Projects in Benin, India, El Salvador and Tanzania. https://www.ilo.org/secsoc/information-resources/publications-and-tools/Discussionpapers/WCMS_207714/lang--en/index.htm.
- International Labour Organization (2009). Convention C187 – promotional framework for occupational safety and health convention, 2006 (no. 187). https://www.ilo.org/dyn/normlex/en/f?p=NORMLEXPUB:12100:0::NO:P12100_ILO_CODE:C187. Accessed 27 December 2018.
- International Labour Organization (2014). *Tackling Informality in E-Waste Management: The Potential of Cooperative Enterprises*. https://www.ilo.org/sector/Resources/publications/WCMS_315228/lang--en/index.htm.
- International Labour Organization (2015a). *Recommendation No. 204 concerning the Transition from the Informal to the Formal Economy*. https://www.ilo.org/ilc/ILCSessions/104/texts-adopted/WCMS_377774/lang--en/index.htm.
- International Labour Organization (2015b). *Small and Medium-sized Enterprises and Decent and Productive Employment Creation*. 1st edn. https://www.ilo.org/ilc/ILCSessions/104/reports/reports-to-the-conference/WCMS_358294/lang--en/index.htm.
- International Labour Organization (2018a). *Women and Men in the Informal Economy: A Statistical Picture*. 3rd edn. https://www.ilo.org/global/publications/books/WCMS_626831/lang--en/index.htm.
- International Labour Organization (2018b). Informal economy: a hazardous activity. https://www.ilo.org/safework/areasofwork/hazardous-work/WCMS_110305/lang--en/index.htm. Accessed 28 December 2018.
- Jonkman, S.N., Godfroy, M., Sebastian, A. and Kolen, B. (2018). Brief communication: loss of life due to Hurricane Harvey. *Natural Hazards and Earth System Sciences* 18(4), 1073-1078. <https://doi.org/10.5194/nhess-18-1073-2018>.
- Kidam, K. and Hurme, M. (2013). Method for identifying contributors to chemical process accidents. *Process Safety and Environmental Protection* 91(5), 367-377. <https://doi.org/10.1016/j.psep.2012.08.002>.
- Kim, Y., Park, J. and Park, M. (2016). Creating a culture of prevention in occupational safety and health practice. *Safety and Health at Work* 7(2), 89-96. <https://doi.org/10.1016/j.shaw.2016.02.002>.
- Krausmann, E., Cruz, A.M. and Salzano, E. (2017). *Natech Risk Assessment and Management: Reducing the Risk of Natural-Hazard Impact on Hazardous Installations*. 1st edn. Amsterdam: Elsevier Inc. <https://www.elsevier.com/books/natech-risk-assessment-and-management/krausmann/978-0-12-803807-9>.
- Krausmann, E. and Salzano, E. (2017). Lessons learned from Natech events. In *Natech Risk Assessment and Management*. Elsevier. Chapter 3. 33-52. <https://doi.org/10.1016/B978-0-12-803807-9.00003-6>.
- Kultida, B., Sunil, H., Cordia, C., Dung, T. and Jakkris, S. (2015). The integration of occupational health and safety into the development of eco-industrial parks. *Health and the Environment Journal* 6(1), 72-84. <http://hej.kk.usm.my/pdf/HEJVol.6No.1/Article06.pdf>.
- Lajini, P. (2014). Importance of workers understanding of chemicals for safety – information, communication and safety culture. *African Newsletter on Occupational Health and Safety* 24(3), 60-61. https://issuu.com/tyoterveyslaitos/docs/african_newsletter_3-_2014_netti.

- Legg, S., Olsen, K., Laird, I. and Hasle, P. (2015). Managing safety in small and medium enterprises. *Safety Science* 71, 189-196. <https://doi.org/10.1016/j.ssci.2014.11.007>.
- Maiguashca, A.F. (2016). How can we save the poor from Latin America's informal economy? 29 April. *World Economic Forum*. <https://www.weforum.org/agenda/2016/04/how-can-we-save-the-poor-from-latin-americas-informal-economy/>. Accessed 27 December 2018.
- Makhonge, P.W. (2014). Situation of chemical safety in small-scale enterprises in Kenya. *African Newsletter on Occupational Health and Safety* 24(3), 54-55. http://ihi.eprints.org/3022/1/Elikana_Lekei.pdf.
- Makino, R. (2016). Stock market responses to chemical accidents in Japan: an event study. *Journal of Loss Prevention in the Process Industries* 44, 453-458. <https://doi.org/10.1016/j.jlp.2016.10.019>.
- Massey, R. (2005). *Building a Healthy Economy: Chemicals Risk Management as a Driver of Development*. Stockholm: Swedish Chemicals Agency. http://www.ase.tufts.edu/gdae/Pubs/rp/KemiReport_05.pdf.
- Massey, R. (2008). Sharing knowledge about chemicals: policy options for facilitating information flow. In *Options for State Chemicals Policy Reform – A Resource Guide*. Coffin, M. and Dunn, M.L. (eds.). Lowell, MA: Lowell Center for Sustainable Production. Chapter 2. 69-96. <http://sustainableproduction.org/downloads/OptionsforStateChemicalsPolicyReform.pdf>.
- Micheli, G.J.L. and Cagno, E. (2010). Dealing with SMEs as a whole in OHS issues: warnings from empirical evidence. *Safety Science* 48(6), 729-733. <https://doi.org/10.1016/j.ssci.2010.02.010>.
- Mizoue, T., Huuskonen, M., Muto, T., Koskinen, K., Husman, K. and Bergstrom, M. (1999). Analysis of Japanese occupational health services for small- and medium-scale enterprises in comparison with the Finnish system. *Journal of Occupational Health* 41, 115-120. http://joh.sanei.or.jp/pdf/E41/E41_2_11.pdf.
- Mrema, E.J., Ngowi, A.V., Kishinhi, S.S. and Mamuya, S.H. (2017). Pesticide exposure and health problems among female horticulture workers in Tanzania. *Environmental Health Insights* 11, 1-13. <https://doi.org/10.1177/1178630217715237>.
- Mukim, M. (2011). *Industry and the Urge to Cluster: A Study of the Informal Sector in India*. Spatial Economics Research Centre (SERC) Discussion Papers. London: London School of Economics and Political Sciences. <http://eprints.lse.ac.uk/33592/>.
- Necci, A., Krausmann, E. and Girgin, S. (2018). *Understanding Natech Risk Due to Storms – Analysis, Lessons Learned and Recommendations*. Joint Research Centre Technical Report JRC112987 (forthcoming). European Commission.
- Nordlöf, H., Wiitavaara, B., Högberg, H. and Westerling, R. (2017). A cross-sectional study of factors influencing occupational health and safety management practices in companies. *Safety Science* 95, 92-103. <https://doi.org/10.1016/j.ssci.2017.02.008>.
- Nyirendaavwil, V., Chinniah, Y. and Agard, B. (2015). Identifying key factors for an occupational health and safety risk estimation tool in small and medium-size enterprises. *International Federation of Automatic Control* 48(3), 541-546. <https://doi.org/10.1016/j.ifacol.2015.06.137>.
- Okoh, P. and Haugen, S. (2014). A study of maintenance-related major accident cases in the 21st century. *Process Safety and Environmental Protection* 92(4), 346-356. <https://doi.org/10.1016/j.psep.2014.03.001>.
- Organisation for Economic Co-operation and Development (2002). *Measuring the Non-Observed Economy: A Handbook*. <http://www.oecd.org/sdd/na/1963116.pdf>.
- Organisation for Economic Co-operation and Development (2003). *Guiding Principles for Chemical Accident Prevention, Preparedness and Response*. <http://www.oecd.org/chemicalsafety/chemical-accidents/guiding-principles-chemical-accident-prevention-preparedness-and-response.htm>.
- Organisation for Economic Co-operation and Development (2012). *Corporate Governance for Process Safety: OECD Guidance for Senior Leaders in High Hazard Industry*. <http://www.oecd.org/env/ehs/chemical-accidents/corporategovernanceforprocesssafety.htm>.
- Organisation for Economic Co-operation and Development (2015). *Addendum Number 2 to the OECD Guiding Principles for Chemical Accident Prevention, Preparedness and Response (2nd Edition) to Address Natural Hazards Triggering Technological Accidents (Natechs)*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2015\)1&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2015)1&doclanguage=en).
- Organisation for Economic Co-operation and Development (2018a). *Guidance on Change of Ownership in Hazardous Facilities*. <http://www.oecd.org/chemicalsafety/chemical-accidents/oecd-guidance-on-change-of-ownership-in-hazardous-facilities.pdf>.
- Organisation for Economic Co-operation and Development (2018b). *Towards an All-Hazards Approach to Emergency Preparedness and Response: Lessons Learnt from Non-Nuclear Events*. <https://www.oecd-nea.org/rp/pubs/2018/7308-all-hazards-epr.pdf>.
- Organisation for Economic Co-operation and Development (2018c). *Developing a Methodology to Quantify the Benefits of Regulations for Chemical Accidents Prevention, Preparedness and Response*. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2018\)3&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2018)3&doclanguage=en).

- Paul, H.L., Antunes, P., Covington, A.D., Evans, P. and Phillips, P.S. (2013). Bangladeshi leather industry: an overview of recent sustainable developments. *Journal of Leather Technologists and Chemists* 91(1), 25-32. https://www.researchgate.net/publication/235609270_Bangladeshi_Leather_Industry_An_Overview_of_Recent_Sustainable_Developments.
- Reniers, G. and Amyotte, P. (2012). Prevention in the chemical and process industries: future directions. *Journal of Loss Prevention in the Process Industries* 25(1), 227-231. <https://doi.org/10.1016/j.jlp.2011.06.016>.
- Reniers, G., Cuypers, S. and Pavlova, Y. (2012). A game-theory based Multi-plant Collaboration Model (MCM) for cross-plant prevention in a chemical cluster. *Journal of Hazardous Materials* 209-210, 164-176. <https://doi.org/10.1016/j.jhazmat.2012.01.004>.
- Rockefeller Foundation (2013). *Health Vulnerabilities of Informal Workers*. <https://assets.rockefellerfoundation.org/app/uploads/20130528214745/Health-Vulnerabilities-of-Informal-Workers.pdf>.
- Rongo, L.M.B. (2005). Health risks related to chemicals used in small scale industries in the informal sector in Dar es Salaam, Tanzania. *East African Journal of Public Health* 2(2), 12-17. <http://www.bioline.org.br/pdf?lp05011>.
- Rongo, L.M.B., Barten, F., Msamanga, G.I., Heederik, D. and Dolmans, W.M.V. (2004). Occupational exposure and health problems in small-scale industry workers in Dar es Salaam, Tanzania: a situation analysis. *Occupational Medicine* 54, 42-46. <https://www.ncbi.nlm.nih.gov/pubmed/14963253>.
- Sebastian, A., Lendering, K.T., Kothuis, B.L.M., Brand, A.D., Jonkman, S.N., van Gelder, P.H.A.J.M., Godfroij, M., Kolen, B., Comes, M., Lhermitte, S.L.M., Meesters, K.J.M.G., van de Walle, B.A., Ebrahimi Fard, A., Cunningham, S., Khakzad Rostami, N. and Nespeca, V. (2017). *Hurricane Harvey Report: A Fact-Finding Effort in the Direct Aftermath of Hurricane Harvey in the Greater Houston Region*. Delft: Delft University Publishers. <https://repository.tudelft.nl/islandora/object/uuid%3A54c24519-c366-4f2f-a3b9-0807db26f69c?collection=research>.
- Seccatore, J., Veiga, M.M., Origliasso, C., Marin, T. and Tomi, G. (2014). An estimation of the artisanal small-scale production of gold in the world. *Science of The Total Environment* 496, 662-667. <http://doi.org/10.1016/j.scitotenv.2014.05.003>.
- Sengupta, A., Bandyopadhyay, D., van Westen, C.J. and van der Veen, A. (2015). An evaluation of risk assessment framework for industrial accidents in India. *Journal of Loss Prevention in the Process Industries* 41, 295-302. <https://doi.org/10.1016/j.jlp.2015.12.012>.
- Singh, T.S., Ratshikhopha, E., Zubaydah, K., Fourie, A., Dikeledi Matuka, O., Bartie, D. and Dayal, P. (2011). Biological and chemical risks in the informal sector. *Occupational Health Southern Africa* 18(6), 4-12. https://www.researchgate.net/publication/278269654_Singh_et_al_Biological_and_chemical_risks_in_the_informal_sector_OHSA_2012.
- Sklet, S (2004). Comparison of some selected methods for accident investigation. *Journal of Hazardous Materials* 111 (2004) 29-37. <https://doi.org/10.1016/j.jhazmat.2004.02.005>.
- Targoutzidis, A., Koukoulaki, T., Schmitz-Felten, E., Kuhl, K., Hengel, K.M.O., Rijken, E., Broek, K. Van den and Klüser, R. (2014). *The Business Case for Safety and Health at Work: Cost-benefit Analyses of Interventions in Small and Medium-sized Enterprises*. European Agency for Safety and Health at Work. <https://doi.org/10.2802/32988>.
- Tauseef, S.M., Abbasi, T. and Abbasi, S.A. (2011). Development of a new chemical process-industry accident database to assist in past accident analysis. *Journal of Loss Prevention in the Process Industries* 24(4), 426-431. <https://doi.org/10.1016/j.jlp.2011.03.005>.
- Taylor, R., May, J., Weyman, A., and Carhart, N. (2017). Understanding organisational and cultural precursors to events. *Proceedings of the ICE -Forensic Engineering*, 170(3), 124-133. <https://doi.org/10.1680/jfoen.17.00006>.
- Thornton, R., Hatt, L., Field, E., Islam, M., Solís, F. and González, M.A. (2010). Social security health insurance for the informal sector in Nicaragua: a randomized evaluation. *Health Economics* 19(1), 181-206. <https://doi.org/10.1002/hecl.1635>.
- United Nations Environment Programme (2010). *A Flexible Framework for Addressing Chemical Accident Prevention and Preparedness: A Guidance Document*. <https://www.preventionweb.net/publications/view/56412>.
- United Nations Environment Programme (2011). *Promoting Safer Operations and Emergency Preparedness in the Value Chain of the Chemical Sector: Case Study on APELL Implementation in China*. <http://apell.ecentre.org/APELLCaseStudyChina.pdf>.
- United Nations Environment Programme (2012). *Analysis of Formalization Approaches in the Artisanal and Small-Scale Gold Mining Sector Based on Experiences in Ecuador, Mongolia, Peru, Tanzania and Uganda*. https://wedocs.unep.org/bitstream/handle/20.500.11822/11357/Formalization_Document_Final_June_2012.pdf?sequence=1&isAllowed=y.
- United Nations Environment Programme (2013). *Global Chemicals Outlook: Towards Sound Management of Chemicals*. http://wedocs.unep.org/bitstream/handle/20.500.11822/20200/unep_global_chemical.pdf?sequence=1&isAllowed=y.

- United Nations Environment Programme (2015). *Chemical Accident Prevention and Preparedness: Case Studies of Implementation*. Paris. http://www.capp.eecentre.org/Upload/files/Case_studies_of_implementation-CAPP.pdf.
- United Nations Environment Programme (2017). *Promoting Chemical Safety Management in Ports and along Transport Routes of Dangerous Goods: Case Studies from Africa*. <https://wedocs.unep.org/bitstream/handle/20.500.11822/20763/Promoting%20Chemical%20Safety%20Management%20in%20Ports%20and%20Transport%20Routes.pdf?sequence=1&isAllowed=y>.
- United Nations Office for Disaster Risk Reduction (2018). *Words into Action Guidelines – Man-Made and Technological Hazards: Practical Considerations for Addressing Man-Made and Technological Hazards in Disaster Risk Reduction*. https://www.unisdr.org/files/54012_manmadetechhazards.pdf.
- United Nations Research Institute for Social Development (2010). Gender inequalities at home and in the market. In *Combating Poverty and Inequality: Structural Change, Social Policy and Politics*. Chapter 4. 107-131. [http://www.unrisd.org/80256B3C005BCCF9/\(httpAuxPages\)/8BACF1B0908D70E1C125778900323600/\\$file/PovRepCh4.pdf](http://www.unrisd.org/80256B3C005BCCF9/(httpAuxPages)/8BACF1B0908D70E1C125778900323600/$file/PovRepCh4.pdf).
- United Nations Research Institute for Social Development (2015). *Sendai Framework for Disaster Risk Reduction 2015-2030*. https://www.preventionweb.net/files/43291_sendaiframeworkfordrren.pdf.
- United States Environmental Protection Agency (2018) Risk Management Plan (RMP) rule, 28 December. <https://www.epa.gov/rmp>. Accessed 1 January 2019.
- Unnikrishnan, S., Iqbal, R., Singh, A. and Nimkar, I.M. (2015). Safety management practices in small and medium enterprises in India. *Safety and Health at Work* 6(1), 46-55. <https://doi.org/10.1016/j.SHAW.2014.10.006>.
- van Oldenborgh, G.J., van der Wiel, K., Sebastian, A., Singh, R., Arrighi, J., Otto, F., Haustein, K., Li, S., Vecchi, G. and Cullen, H. (2017). Attribution of extreme rainfall from Hurricane Harvey, August 2017. *Environmental Research Letters* 12, 12. <https://doi.org/10.1088/1748-9326/aa9ef2>.
- Vasina, M. (2018). *Health-related Practices and Perceptions among Waste Pickers. The Case of Mbeubeuss Waste Dump in Senegal*. Geneva: Graduate Institute of International and Development Studies. http://www.wiego.org/sites/default/files/resources/files/VASINA_Marine_Dissertation_Compressed.pdf.
- Veiga, M.M., Angeloci-Santos, G. and Meech, J.A. (2014). Review of barriers to reduce mercury use in artisanal bold mining. *The Extractive Industries and Society* 1(2), 351-61. <https://doi.org/10.1016/j.exis.2014.03.004>.
- Verbano, C., Venturini, K. and Venturini, K. (2013). Managing risks in SMEs: a literature review and research agenda. *Journal of Technology Management & Innovation* 8(3), 33-34. <https://doi.org/10.4067/S0718-27242013000400017>.
- World Health Organization (2018). *Chemical Releases Caused by Natural Hazard Events and Disasters: Information for Public Health Authorities*. <https://www.who.int/ipcs/publications/natech/en/>.
- Yuan, X. and Wang, K. (2012). Study on safety management of small and medium-sized enterprises based on BBS. *Procedia Engineering* 45, 208-213. <https://doi.org/10.1016/j.PROENG.2012.08.145>.
- Zhao, J., Joas, R., Abel, J., Marques, T. and Suikkanen, J. (2013). Process safety challenges for SMEs in China. *Journal of Loss Prevention in the Process Industries* 26(5), 880-886. <https://doi.org/10.1016/J.JLP.2012.09.003>.
- Zheng, X., Xu, X., Akangbe Yekeen, T., Zhang, Y., Chen, A., Kim, S.S., Dietrich, K.N., Ho, S.-M., Lee, S.-A., Reponen, T. and Huo, X. (2016). Ambient air heavy metals in PM2.5 and potential human health risk assessment in an informal electronic-waste recycling site of China. *Aerosol and Air Quality Research* 16, 388-397. <https://doi.org/10.4209/aaqr.2014.11.0292>.
- Zock, J.P. (2005). World at work: cleaners. *Occupational and Environmental Medicine* 62, 581-584. <https://doi.org/10.1136/oem.2004.015032>.

Chapter 7

Bern University of Applied Sciences (2017). *Response-Inducing Sustainability Evaluation (RISE)*. https://www.haf1.bfh.ch/fileadmin/docs/Forschung_Dienstleistungen/Agrarwissenschaften/Nachhaltigkeitsbeurteilung/RISE/What_is_RISE.pdf.

Bey, N. (2018). Life cycle management. In *Life Cycle Assessment: Theory and Practice*. Hauschild, M.Z., Rosenbaum, R.K. and Olsen, S.I. (eds.). Cham: Springer. 519-544. http://doi.org/10.1007/978-3-319-56475-3_22.

European Commission (2010). Directive 2010/75/EU of the European Parliament and of the Council of 24 November 2010 on industrial emissions (integrated pollution prevention and control). *Official Journal of the European Union* L (334), 17-119. <http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX:32010L0075>.

European Commission (2013). Commission Recommendation 2013/179/EU of 9 April 2013 on the use of common methods to measure and communicate the life cycle environmental performance of products and organisations. *Official Journal of the European Union* L (124), 1-210. <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32013H0179>.

- Fantke, P., Ernststoff, A.S., Huang, L., Csiszar, S.A. and Jolliet, O. (2016). Coupled near-field and far-field exposure assessment framework for chemicals in consumer products. *Environment International* 94, 508-518. <http://doi.org/10.1016/j.envint.2016.06.010>.
- Fantke, P. and Ernststoff, A. (2018). LCA of chemicals and chemical products. In *Life Cycle Assessment*. Hauschild, M.Z., Rosenbaum, R.K. and Olsen, S.I. (eds.). Cham: Springer International Publishing. 783-815. https://doi.org/10.1007/978-3-319-56475-3_31
- Fantke, P., Huang, L., Overcash, M., Griffing, E. and Jolliet, O. (2019). Toward a life-cycle based alternatives assessment. In *Green Chemistry* (submitted).
- Hauschild, M.Z. (2005). Assessing environmental impacts in a life-cycle perspective. *Environmental Science and Technology* 39, 81A-88A. <http://doi.org/10.1021/es053190s>.
- Hauschild, M., Huijbregts, M.A.J. (eds.) (2015). *Life Cycle Impact Assessment*. Dordrecht: Springer. <https://doi.org/10.1007/978-94-017-9744-3>.
- Hellweg, S. and Milà i Canals, L. (2014). Emerging approaches, challenges and opportunities in life cycle assessment. *Science* 344 (6188), 1109-1113. <http://doi.org/10.1126/science.1248361>.
- Henderson, A.D., Hauschild, M.Z., van de Meent, D., Huijbregts, M.A.J., Larsen, H.F., Margni, M., McKone, T.E., Payet, J., Rosenbaum, R.K. and Jolliet, O. (2011). USEtox fate and ecotoxicity factors for comparative assessment of toxic emissions in life cycle analysis: sensitivity to key chemical properties. *International Journal of Life Cycle Assessment* 16, 701-709. <http://doi.org/10.1007/s11367-011-0294-6>.
- Hottle, T.A., Bilec, M.M. and Landis, A.E. (2013). Sustainability assessments of bio-based polymers. *Polymer Degradation and Stability* 98, 1898-1907. <http://doi.org/10.1016/j.polymdegradstab.2013.06.016>.
- International Organization for Standardization (2018). ISO 14000 family – environmental management. <https://www.iso.org/iso-14001-environmental-management.html>. Accessed 28 December 2018.
- Ny, H., MacDonald, J.P., Broman, G., Ryoichi, Y. and Robert, K.-H. (2006). Sustainability constraints as system boundaries: an approach to making life-cycle management strategic. *Journal of Industrial Ecology* 10, 61-77. <http://doi.org/10.1162/108819806775545349>.
- Pivnenko, K. and Astrup, T.F. (2016). The challenge of chemicals in material lifecycles. *Waste Management* 56, 1-2. <http://doi.org/10.1016/j.wasman.2016.08.016>.
- Ridoutt, B., Fantke, P., Pfister, S., Bare, J., Boulay, A.-M., Cherubini, F., Frischknecht, R., Hauschild, M., Hellweg, S., Henderson, A., Jolliet, O., L'vasseur, A., Margni, M., McKone, T., Michelsen, O., Milà i Canals, L., Page, G., Pant, R., Raugei, M., Sala, S., Saouter, E., Verones, F. and Wiedmann, T. (2015). Making sense of the minefield of footprint indicators. *Environmental Science & Technology* 49, 2601-2603. <http://doi.org/10.1021/acs.est.5b00163>.
- Rosenbaum, R.K., Huijbregts, M.A.J., Henderson, A.D., Margni, M., McKone, T.E., van de Meent, D., Hauschild, M.Z., Shaked, S., Li, D.S., Gold, L.S. and Jolliet, O. (2011). USEtox human exposure and toxicity factors for comparative assessment of toxic emissions in life cycle analysis: sensitivity to key chemical properties. *The International Journal of Life Cycle Assessment* 16, 710-727. <http://doi.org/10.1007/s11367-011-0316-4>.
- United States Environmental Protection Agency (2014). *Climate Change Adaptation Implementation Plan*. The Office of Chemical Safety and Pollution Prevention (OCSPP). <https://19january2017snapshot.epa.gov/sites/production/files/2016-08/documents/ocspp-climate-change-adaptation-plan.pdf>.
- The Natural Step (2018). Bring strategic sustainability into your product design and innovation. <https://thenaturalstep.org/slca>. Accessed 1 January 2019.
- Verones, F., Bare, J., Bulle, C., Frischknecht, R., Hauschild, M., Hellweg, S., Henderson, A., Jolliet, O., Laurent, A., Liao, X., Lindner, J.P., Maia de Souza, D., Michelsen, O., Patouillard, L., Pfister, S., Posthuma, L., Prado, V., Ridoutt, B., Rosenbaum, R.K., Sala, S., Ugaya, C., Vieira, M. and Fantke, P. (2017). LCIA framework and cross-cutting issues guidance within the UNEP-SETAC Life Cycle Initiative. *Journal of Cleaner Production* 161, 957-967. <http://doi.org/10.1016/j.jclepro.2017.05.206>.

